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THE DISEASES OF CHILDREN

A WORK FOR THE PRACTISING PHYSICIAN

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IN FIVE VOLUMES

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VOL. II.

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THE DISEASES OF CHILDREN

DISEASES OF THE NEWBORN

BY
DR. W. KNÖPFELMACHER, OF VIENNA

TRANSLATED BY
DR. A. S. MASCHKE, CLEVELAND, O.

I. BIRTH INJURIES

THE fœtus is exposed to many injuries during its passage into the world besides those directly dependent on the act of labor. A part of these injuries are attributable to the physician or nurse, some are dependent on a disproportion between the size of the child and the width of the pelvis, others are due to disturbance of the placental blood supply from contraction of the uterus and compression of the cord.

The physician should make a careful examination of every newborn infant to ascertain whether any birth injuries have occurred. The majority of injuries are found in cases where no artificial aid has been employed. Dittrich classifies birth injuries as follows:

1. Abrasions of the skin.
2. Ecchymoses of the skin.
3. Wounds of the soft parts.
4. Fractures and injuries of the bones.
5. Ruptures of internal organs.
6. Tearing off entire portions of the body.

Abrasions and open wounds of the cutaneous surface may be produced by the finger of the examining physician or midwife; by instruments or through the pressure of the bony pelvic ring and possibly by exostoses or tumors of the latter.

The pressure marks caused by projecting parts of the pelvic rim, especially the promontory, are of especial value to the accoucher, giving information concerning the fœtal presentation and the mechanism of labor; they form more or less intensive areas of redness in the skin, striated and often containing hæmorrhages. In case the pressure operates for a longer time necrosis of the skin occurs as a result of the interference with its nutrition. These pressure marks occur most often with vertex presentations.

The application of forceps often leads to circumscribed compressions over the cranial and facial bones and in consequence to suggillations and œdemas, excoriations and sometimes necroses of the skin.

The wounds of the skin, covered with granulations, which are occasionally encountered in children immediately after birth must be ascribed to the tearing away of earlier formed adhesions of the skin to amniotic bands.

Hæmorrhages occur frequently in unassisted as well as assisted labors. They are in part traumatic in origin, in part, however, due to interruption in the placental circulation through compression of the cord, or to asphyxia. The hæmorrhages into the skin are mostly only punctate and very rarely assume larger proportions. Among the hæmorrhages of other organs the most frequent are cephalæmatomata, and hæmatomata of the sternocleidomastoid muscle, which will be taken up in detail later; also hæmorrhages of the cranial and spinal meninges and into the substance and cavities of the brain and cord.

Fig. 1.

Injury to soft tissues of the head as a result of improperly applied forceps.

Meningeal and cerebral hæmorrhages are frequent, as a rule, giving rise to no symptoms; only occasionally symptoms of increased intracranial pressure—evident cerebral compression, slowing of the pulse, arrhythmic, superficial, intermittent respirations; protuberant or tense fontanelle, convulsions, and paralysis—are observed immediately after birth. Many of these children are apparently born dead, some are normal at first but on the second or third day the breathing becomes shallow (Kundrat) and the children die with the manifestations of asphyxia or pulmonary atelectasis.

Convulsions.—In less acute cases attention is called to the meningeal bleeding by the occurrence of eclamptic attacks. The spasms may be bilateral or unilateral or may, moreover, be limited to a single extremity, to one half of the face or to the eyes. They may cease occurring after a short time (just as the paralysis) or continuing, be the indicator of a permanent disturbance of the cerebral function.

We are doubtless justified, in occasional cases, in holding birth injuries responsible for permanent impairment of the brain function

of the nature of epilepsy, paralyses, idiocy, etc. (Concerning this question reference is made to the chapter on Nervous Diseases.)

The **diagnosis** of meningeal hæmorrhages in the newborn might probably be confirmed by lumbar puncture; Finkelstein was fortunate enough to accomplish this in one case. The drawing off, on puncture, of a hæmorrhagic fluid does not suffice for making a diagnosis, as this might be due to the puncturing of a vessel. One must find red cells which are altered morphologically, possibly casts or cell detritus. Kundrat has written explicitly concerning hæmorrhages localized in the meninges.

According to his investigations the hæmorrhages are usually situated under the arachnoid and in the tissues of the pia; less frequently subdural hæmorrhages are found along with these. Occasionally intrameningeal hæmorrhages occur over the cerebellum and rarely into the lateral ventricles. As a rule there are no hæmorrhages in the substance of the brain itself. According to Kundrat, these hæmorrhages regularly occur in the same manner: during the passage of the fœtus there is compression of the head, over-riding of the cranial bones, tension on and tearing of the vessels or occlusion of the falciform sinus, stasis in the veins emptying into this sinus and tearing of these veins.

The hæmorrhages into the lateral ventricles are probably due to tearing of the vena magna Galeni.

Hæmorrhages in other organs, such as the muscles, the lungs and the chorioid membrane (Sidler-Huquenin) have been often reported as consequences of birth traumata.

Fractures of the long bones and the clavicle are most frequent amongst the *injuries to the bones*. They are, moreover, not uncommon in unassisted labor. Separation of the epiphysis of the humerus has been found at times.

Dislocations are less common; that of the shoulder occasionally, and rarely of the hip-joint.

Fractures and dislocations of the inferior maxilla and of the clavicle are among the rarest of birth injuries.

The changes that occur in the *cranial bones* are especially important. The commonest result of birth trauma is overlapping of the cranial bones. The parietal bones lap over the occipital or the frontal and possibly one parietal bone over the other. This overlapping usually disappears within a few days after birth. It is brought about by the disproportion between the cranial and pelvic diameters; the various fœtal positions show constantly recurring types of cranial overlapping. Changes in the shape of the cranium, either as a flattening or a bulging, occur in many cases (according to Litzmann, in 45 per cent.). The sacral promontory especially exerts pressure on the contiguous cranial

bones and thus flattens them out; with this comes an increased bending of the bone opposite, against the symphysis.

Depressions of the skull are serious occurrences. One recognizes grooved and spoon (or funnel) shaped depressions; they are usually produced by pressure of the promontory, seldom by the symphysis or by an exostosis.

The flat pelvis rather than the generally contracted pelvis produces these indentations; they may be caused by the pressure of forceps or, it is said, by a prolapsed arm or leg. The deeper depressions are, as a rule, combined with very slight fractures of the external table of the skull.

Cephalæmatomata commonly occur at the site of spoon-shaped impressions. Spoon-shaped impressions offer a more unfavorable prognosis than the gutter-shaped ones, often leading to death and occasionally to cerebral complications, as for example convulsions.

The attempt to relieve these depressions by operation has been made time and again. Trephining and also elevation by means of a suction apparatus have been recommended. Munro Kerr suggests the possibility of forcing out the depression by compression anteroposteriorly.

Fractures of the cranial bones, lacerations of the sutures and tearing off of the condyloid processes of the occipital bone from its tabular portion are rare happenings due to the injudicious pulling in cases of contracted pelvis.

In the following sections the most important birth injuries are taken up in detail.

A. CAPUT SUCCEDANEUM
(head-swelling, breech-swelling)

Swellings occurring on the presenting part, as the result of compression, are constant sequelæ of parturition.

The presenting part, during its passage, is tightly squeezed by the soft parts, especially by the pelvic diaphragm (Stumpf) and the external os of the uterus; this ligature of the presenting part causes disturbance in the circulation of blood and lymph, and thereby a stasis arises, with outpouring of blood and serum into the tissues. The whole of the child's body except the part in front of the ligature is under an increased pressure, possibly thus producing suction on the presenting part. When the vertex presents, there is a swelling of a doughy consistency, brought about by œdema of the soft parts, usually over one parietal bone and in fact usually over its hinder portion or else over the upper part of the tabular portion of the occipital bone. This consists of a sero-hæmorrhagic infiltration of all the tissues, the greater part of the transudation being between the galea and the periosteum

(Lönnberg). Countless small hæmorrhages are always present in the tissues, likewise in the periosteum; at times there is hyperæmia of the substance of the bone and even of the meninges beneath the swelling. In cases where the labor is of short duration the swellings are only slightly developed. The factors determining the size of a caput succedaneum are the size of the fœtal head, the dimensions of the maternal pelvis and the duration of the labor. A caput succedaneum can hardly be confused with a cephalæmatoma, as the former is not limited by the suture bones; it is also, as a rule, more diffuse and pits on pressure with the finger.

With breech presentations there exists a swelling of the scrotum and penis, or, in the female, of the labia or nates. This swelling is also not entirely made up of serous effusion but contains many small hæmorrhages.

Birth-swellings occur in a similar manner on the face or on the extremities, if these are the presenting parts.

B. CEPHALÆMATOMA

Hæmorrhage under the galea aponeurotica in the newborn was given this name by Naegele.

Cephalæmatomata occasionally develop during labor, usually, however, some time after birth as a consequence of subperito-osteal hæmorrhage. They usually develop between the second and fourth day of life, rarely as late as the second week.

Cephalæmatomata were encountered 99 times in 20,000 births at the Munich Lying-in Hospital (F. Beck). They have their seat of predilection over the parietal bone, are usually unilateral and are moreover on the right side in the majority of instances. They occur at times over both parietal bones or over other cranial bones, such as the frontal, occipital and temporal; occasionally several subperiosteal hæmatomata are found in the same child.

On examination, a rounded mass, varying in its degree of convexity, is found over the diseased bone; the skin over the tumor is movable and either normal or, in the first days of life, œdematous. At times there are hæmorrhages or pressure marks.

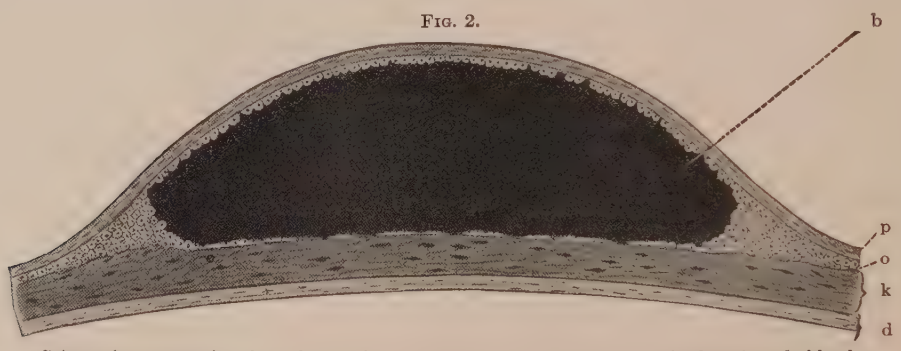
During the first days the skin is usually tense; this tension, however, gradually diminishes and the tumor shows distinct fluctuation. It occupies a larger or smaller part of the parietal bone *but never oversteps the boundaries set by the sutures of the bone;* inasmuch as the periosteum is especially adherent at the sutures, the extravasated blood is unable to separate the pericranium from the bone at these points. The swelling varies in size from that of a nut to that of a goose egg and larger. It grows during the first days after birth, attaining its maximum at the end of the first week.

On palpating the tumor, by passing the finger over it from periphery to dome, the impression of a groove or defect in the cranium can be felt. This impression comes from the tumor being surrounded by a hard wall-like ring of newly-formed bony tissue. In its further course the tumor becomes flatter, the wall-like ring which grows from the edge towards the centre becomes broader until the whole mass is covered with a shell of newly-formed bony tissue, more or less dense. Then the tumor acquires a parchment-like sensation, distinctly crepitating on pressure over the bony shell.

In other cases practically no new growth of bone occurs or else only at the margin of the effusion; the blood is then more rapidly absorbed and the periosteum settles flush with the bone.

The formation of the bony ring becomes comprehensible when one considers that the hæmorrhage originates in the torn vessels of the highly

Fig. 2.



Schematic cross-section through cephalæmatoma of about two to three weeks duration : b, blood; p, periosteum; o, infiltration with osteophytes; k, bony tissue; d, dura mater.

vascular osteogenetic tissue which lies next to the connective tissue layer of the periosteum. The bleeding not only elevates the periosteum but also a portion of the osteogenetic zone. Hence arises the new growth of bone which is most marked at the margin and forms the wall which, at times totally, at times (with large effusions) only partially, covers the swelling. The periosteal growth begins usually by the end of the first week; up to this time no wall is palpable. The retrogression of the tumor follows sometimes quickly and sometimes slowly. The absorption of the blood may occur quickly without the distinct formation of new bone; in other cases the absorption of the effusion and the resolution of the tissues takes several weeks, usually six to eight and sometimes even much longer.

The bone is either unchanged after the healing of a cephalæmatoma or else presents a slight periosteal thickening.

Complications.—Cephalæmatomata do not always progress so smoothly. Occasionally the bloody contents of the swelling become infected. The infection usually occurs from an external wound; in

rare cases its cause is unknown; sometimes, however, it is the result of an incision into the mass. Abscess formation then occurs, which is a serious matter because the purulent inflammation may extend to the denuded bone or to the soft parts of the skin, whose movable, wide-meshed cellular tissue furnishes opportunity for the spreading of the pus and the extension of the inflammation. Both these complications can become very dangerous; the first by causing an osteitis and extension to the meninges and the second by causing sepsis.

Accompanying cephalæmatomata there is found, very rarely, an effusion of blood on the under surface of the cranial bone, thus separating the dura from it (*cephalœmatoma internum*). This may occur either with or without a fracture of the bone; in the latter case the blood flows to the under surface of the bone through a congenital fissure. Signs of increased intracranial pressure may then possibly arise, which, however, may be caused in like manner by a simultaneous cerebral or meningeal hæmorrhage.

Pathology.—In children dying immediately after birth, the skin over the cephalæmatoma is œdematous and richly besprinkled with hæmorrhages. The periosteum is elevated, darkly discolored and also full of small hæmorrhages; between it and the bare, rough bone the dark fluid is gathered and a few clots of fibrin cling to the walls.

In cases in which the child dies some time after birth, there are signs of a periosteal growth of new bone either at the margin of the effusion, or later, also on the inner surface of the whole roof of the tumor; this is soft at first, offering no resistance to the knife; but later it becomes hard and then colloid masses or irregular lamellæ of new bone are found over the bone.

With *cephalœmatoma internum* similar anatomical changes are found with the addition of the signs of a fracture or else evidence to show that the blood has trickled through a pre-existing fissure. In some cases there are also cerebral hæmorrhages. With complications, conditions are encountered, often extensive, corresponding to the clinical picture.

Pathogenesis.—Cephalæmatomata are caused by a tearing of the vessels of the subperiosteal zone, with the pouring forth of blood and the resultant elevation of the periosteum. The bursting of a vessel is as a rule, caused by stasis and hyperæmia (M. Runge).

Because the vessels are easily torn and the periosteum is loosely connected with the bones of the skull in the newborn, stasis readily leads to the formation of a cephalæmatoma. This simple explanation of Runge's makes it easy to understand just why the parietal bone and especially the right parietal bone should so often be the seat of cephalæmatoma. This is due to the preponderance of L. O. A. positions, with which the right parietal bone presents, so that stasis and the

bursting of vessels take place oftenest over it. Whether, in this event, only small hæmorrhages or a cephalæmatoma ensues depends principally upon the size of the ruptured vessels.

Another theory (Fritsch) states that stasis is not so much responsible for the occurrence of a cephalæmatoma as is the mechanical loosening of the periosteum by means of a trauma, such as may occur, moreover, during the course of normal labor. The fœtal head becomes fixed in the birth canal and the scalp sticks tightly to the maternal soft parts; in the interim between pains the head recedes, thus pulling on the scalp and separating the periosteum from the cranium.

Other authors assume only a localized pressure operating on the cranium with a resultant rupture of blood vessels. Runge's explanation is the most plausible; but it must be conceded that the assumption of a pressure operating locally, makes the explanation more easily understandable. Otherwise it would not be possible to explain the occurrence of cephalæmatoma in places where the blades of forceps have pressed on the head. The cases, happily rare, where a fracture has been followed by a cephalæmatoma also argue for this. In the vast majority of instances, however, cephalæmatomata occur in uneventful, uncomplicated labors.

From a large number of observations concerning the circumstances under which cephalæmatomata occur the following conclusions are drawn by F. Beck.

Cephalæmatomata occur most frequently over the right parietal bone; four-fifths of all cases occur in primiparæ; primiparæ constitute about one-half of all births. The rigidity of the maternal soft parts has, therefore, a considerable influence; this is also shown by the fact that the cephalæmatomata occur more frequently in the children of elderly primiparæ than those of younger mothers. Slightly contracted maternal pelves, abnormal fœtal positions and premature rupture of the amniotic sac are of importance since thereby the head may be easily subjected to irregularly or sporadically applied pressure.

The infants in whom cephalæmatomata occurred were, for the most part, full-term children, but premature infants are not immune. It is a striking fact that all statistics show a substantial preponderance of male over female infants (about two to one); this probably depends on the larger head measurements in male children. A considerable number of the children are born asphyctic; asphyxia conduces to the formation of cephalæmatoma by causing increased hyperæmia and also because of the fact that under its influence the nutrition of the vessel walls suffers.

The **diagnosis** is in general easily established. Only in the first days, a caput succedaneum, which often accompanies a cephalæmatoma, may possibly cause doubt. It is easily differentiated from trau-

matic meningocele since the latter swells when the child cries and can be emptied by pressure. A cephalæmatoma subaponeuroticum, a hæmorrhage between the scalp and the periosteum, is easily differentiated from the subperiosteal form by the fact that it is not limited by the suture lines, which it oversteps.

The **prognosis** is good. Complications are rare.

The **therapy** as a rule should be conservative. Protection from pressure by means of heavy cotton padding fixed by means of a hood, almost always insures a nice healing of the swelling. Incision is to be considered only in the cases where the tumor is very large; and here, under the strictest asepsis, it is to be preferred to all other procedures. The majority of physicians, however, rightly oppose operative interference since thereby the danger of infection is substantially increased. Incision must be employed, however, in every case where *the skin over the swelling becomes red and œdematous;* for then there is suppuration of the effusion and only timely and thorough opening and dressing with dermatol gauze or other antiseptics can halt the spread of the inflammation. The employment of puncture for the purpose of emptying the blood and the use of compression bandages are not recommended; it is very difficult to apply bandages which really exert compression and this procedure is apt to injure the scalp.

C. HÆMATOMA AND MYOSITIS OF THE STERNOCLEIDOMASTOID MUSCLE

Dieffenbach first described this condition in 1830 and also first brought out its causal relation with congenital wry neck.

Symptoms.—Soon after birth, or a few days later, a tumor, of a hard, cartilage-like consistency, is found in the sternocleidomastoid muscle and moreover usually in its sternal portion; the tumor varies in size from that of a hazel-nut to that of a pigeon egg and over it the skin is usually unchanged although at times œdematous. When the muscles are relaxed the tumor is easily movable with the sternomastoid; it is not painful, although at times tender on pressure. In some instances the chin is pointed toward the healthy side, in some toward the diseased side and in others the positon of the head is normal. The general health is not disturbed.

Nature and Pathological Anatomy.—In this condition we have to deal with a tearing of the fibres of the sternomastoid with a consequent bleeding. The blood flows under the muscle-sheath and between the torn fibres; in cases of considerable duration it is possible to demonstrate, microscopically, the partial disappearance of the muscle fibres and proliferation of young connective tissue.

Occurrence and Pathogenesis.—The disease, in the majority of instances, occurs in children delivered without the aid of instruments.

The right side is more often affected than the left, in rare instances both sternomastoids are affected. The disease occurs most often with breech presentations, less often with vertex presentations. In cases of unassisted labor the occurrence of the hæmatoma must be attributed to an extreme traction on the sternomastoid; this traction can take place only from an excessive rotation of the head (Küstner) and moreover the sternomastoid which remains inactive during the act of rotation is subjected to the greater traction; therefore the muscle affected corresponds to the side towards which the head is rotated. In assisted labor also, rotation of the head is responsible for the tearing of the muscle although pressure of the forceps, of the fingers of the accoucheur or of the cord wound round the neck are said to be able to produce this lesion.

The **prognosis** is good. The tumor usually disappears spontaneously within a few (4–8) weeks. Proof is wanting that a permanent wry neck ever develops from this condition.

The **treatment** consists in massage of the diseased muscle, carried out very gently, for several minutes daily. In case the disease has existed for some time and wry neck has developed, it is recommended to employ passive movements of the head, in the sense of rotation away from the affected side.

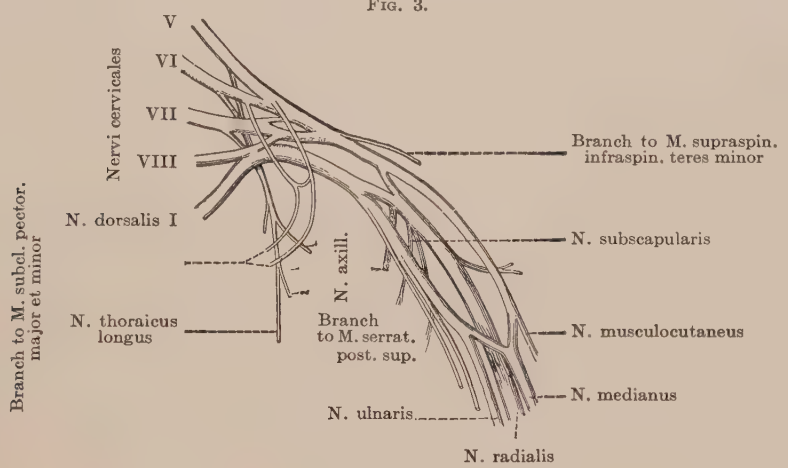
D. OBSTETRICAL PARALYSES

From the large category of paralyses caused by injury to the newborn during parturition, there are classified under the title obstetrical paralyses, only those confined to the upper extremity and due to injury of the brachial plexus. Its symptom-complex is identical with plexus paralysis in the adult and it deserves special consideration only on account of its etiology and the regularity of the nervous symptoms following the birth-trauma. Duchenne accurately described the disease and Erb elucidated its nature. Subsequent authors have only substantiated the results of the studies and observations of the above named and have broadened and deepened our knowledge of the clinical manifestations and pathogenesis of the disease.

Symptoms.—Inactivity is noticed in the diseased arm immediately after birth. Whereas the healthy extremity, especially shortly after birth, shows a rather marked rigidity of its musculature and whereas the child executes various more or less extensive movements, with it, the diseased arm hangs relaxed, and it is impossible, by pricking the skin to elicit active lifting of the arm at the shoulder or flexion of the elbow. The shoulder hangs somewhat lower than the unaffected one; this is less marked in very recent cases than in older ones. The upper arm is rotated inwards and the forearm pronated so that the palm of the hand is turned more or less outwards. The movements of the scapula

are either not interfered with at all or else only slightly. Supination in the elbow-joint is always absent; the wrist-joint seems either free from involvement or else extension is limited, flexion remaining possible. The finger-joints as a rule are free from disturbances although rarely they suffer limitation in flexion. The sensibility is either undisturbed or there may be disturbances of sensation in the distribution of the musculocutaneous and more rarely the axillary nerve (Oppenheim); even with very extensive paralyses, the sensibility on the inner surface of the arm remains normal (Klumpke). Tests of the electrical reactions in the newborn give, in general, results of but little practical value, since the irritability is physiologically less as compared with older children and adults, and the contractions themselves, physiologically, tardy and vermiform (C. Soltmann and A. Westphal). The reaction of degeneration and other similar reactions are not to be employed in the

Fig. 3.



Brachial plexus.

same sense as in the adult. The form of the disease described as the type, by Duchenne and Erb, is the most frequent, occurring according to Stransky in 80 per cent. of all cases. The disease depends upon a peculiar combination of muscle-palsies which is manifest in all these cases and the rationale of the occurrence of which was rightly recognized by Erb. The following muscles are involved: deltoid (lifter of the arm), biceps (flexor of the forearm), infraspinatus (external rotator of arm) supinator longus (flexor, possibly supinator of the forearm) and supinator brevis (supinator of the forearm). These muscles are supplied by the brachial plexus which is formed by branches of the four lower cervical and the greater part of the first dorsal nerves. Erb found a point corresponding to the point where the sixth cervical nerve emerges between the musculi scaleni, from which point it is possible with the faradic current, to produce, simultaneously, contractions in the above-

APPENDIX

Besides the typical obstetrical paralysis of the upper extremity, injuries to other nerves occur, most frequent among which is a peripheral facial paralysis. This may be uni- or bilateral; all or only one of the branches of the facial nerve may be involved. The paralysis occurs as a rule in instrumental labor as a result of the pressure of the blade of the forceps on the trunk of the facial nerve. It occurs only very exceptionally in unassisted labor. It may be caused by an œdema or a hæmatoma in the trunk of the facial nerve, which has been produced by the pressure of the bony pelvic ring, in cases of contracted pelvis.

The **diagnosis** is made as in facial paralysis from other causes (which see); the possibility of the paralysis being central (*e.g.* from congenital cerebral paralysis or congenital mal-development of the facial muscles) must be considered in every case. The prognosis is relatively a good one. The paralysis disappears in the most instances within a few months.

Obstetrical paralyses of the lower extremities have not often been observed. Injuries and tears of the spinal cord occur only with excessively energetic attempts at extraction and as a rule lead to the death of the child. Hæmorrhages into the spinal cord, with rare exceptions, give rise to no clinical symptoms.

II. DISTURBANCES RESULTING FROM THE CHANGE TO EXTRA-UTERINE LIFE

A. ALBUMINURIA AND URIC ACID INFARCTION OF THE NEWBORN

In the first days of its life the infant passes but little urine; the scanty ingestion of fluids and the active loss of water through the skin and lungs reduce the kidney-secretion to a level lower than that corresponding to the body weight. Regular examinations of the urine show the striking fact that albumin is present for one or more days in the urine of at least one half of all newborn infants and according to the latest investigations in all. This albumin is nucleo-albumin; more rarely some other proteid substance (Flensburg). The assumption that mucin is present in the urine of newborn children (Cruse) has not been substantiated. The amount of albumin varies but is never large. The excretion of albumin begins after birth (urine found in the bladder at birth is usually free from albumin), lasts rarely only one, usually the first four days and is, as a rule, ended within the first nine days of life (Cruse). In very rare cases it has been known to persist as long as the second month of life.

The **cause** of this albuminuria has not been definitely settled. It possibly has a connection with infarction of the kidney in the newborn (Hofmeister); at least it is true that the height of the infarct formation is often accompanied by considerable albuminuria (Flensburg). The

absence of urates does not argue against this, since infarctions may be present in the kidney without there being anything demonstrable in the urine. With this assumption as a basis one could attribute the nucleo-albumin of the newborn to some damage to the parenchyma of the kidney by uric acid infarction. Nucleo-albumin does not come from the blood, since none is present there; it has its origin in the cells of the parenchyma of the kidney. The question, whether albuminuria in the newborn is a physiological process which, according to Virchow, depends on revolutionary changes in the metabolism of the newborn at the moment of birth, remains, according to Czerny and Keller, as yet undecided.

The urine of the newborn is clear, immediately after birth; later, however, it usually is cloudy and remains so for 4–5 days. Microscopically the urinary sediment shows the presence of pavement epithelium from the peripheral urinary passages, also leucocytes, hyaline and epithelial casts, renal epithelium and amorphous hyaline substance (Cruse, Flensburg). According to Rensing, casts are present in the urine of 39.4 per cent. of breast-fed children and only 9.1 per cent. of artificially fed children. This is connected with the larger ingestion of fluids by the children fed on cow's milk, who thus secrete a less concentrated urine which is less damaging or irritating to the kidney epithelium. Finally a brick-red sediment appears in the urine, often even on the first day, but usually on the second to the fourth, which according to Flensburg has been analyzed by Sjöqvist and found to be composed of urate of ammonium; with a hyaline substance for a nucleus it gathers in rods or balls and often contains incrusted epithelial cells or casts. This sediment owes its origin to the *uric acid infarctions of the newborn.* It is only excreted during the first days of life, usually from the second to the fourth day and rarely later than the beginning of the second week. According to Flensburg these infarcts are present in all newborn children. Where they are present in considerable proportions brick-red spots are seen on the diaper of the child; retention of urine in the newborn seems sometimes to be connected with the elimination of infarctions. In this case the first urine is voided without difficulty, but later retention and restlessness set in and may persist for many hours.

Uric acid infarctions are rarely found in the kidneys of still-born infants. In children who have lived for a time, however (hours, days or weeks), one exceptionally often finds that the pyramids alone of the kidney are striped with a large number of reddish- or brownish-yellow, often also light yellow lines; under the microscope these turn out to be balls, granules or rods of uric acid salts embedded in an organic, proteid-like substance. Virchow considered the urate to be the ammonium salt. The occurrence of these infarcts has not yet been explained. It

is true that Rensing, Sjöquist and others have established the very high percentage of uric acid in the urine of the newborn; since however, in adults with very high percentages of uric acid, *e.g.* in cases of leukæmia, infarctions have never been described; it becomes necessary to assume other peculiar relations in order to explain the infarct formation. Flensburg believes that a proteid-like substance is secreted in fœtal life and during the first days after birth, which gathers in the convoluted tubules, interferes with the passing off of the urine and becomes incrusted from the passage of the urine rich in uric acid. Spiegelberg was able to show that uric acid infarctions follow the injection of urates in newborn animals but never in adults. The explanation of this was not forthcoming from his researches.

B. PREGNANCY-REACTIONS IN THE NEWBORN AND THE DISTURBANCES ARISING THEREFROM

After birth, in the body of the infant certain peculiar conditions are noticeable which we designate, with J. Halban, "pregnancy-reactions," since they are connected with the circulation of certain bodies in the blood of the pregnant woman and with the carrying of these substances over into the blood of the fœtus. Hence we find changes in the newborn which entirely disappear within the first weeks of life, never to recur in the male, and in the female only during puberty and pregnancy.

I. SECRETION OF THE MAMMARY GLAND IN THE NEWBORN

Symptoms.—On about the second or third day, rarely later, one notices almost invariably in every newborn child, without regard to sex, a swelling of the breast which increases on the following days and usually reaches its acme from the eighth to the twelfth day. From this time on the swelling gradually diminishes and disappears completely in the third or fourth week. The skin is entirely unchanged over the swelling. On squeezing the gland a milky secretion exudes which is called "witch's milk." This secretion has been examined repeatedly and contains much albumin, casein, fat, milk-sugar, and salts; its ash contains chlorine, phosphoric acid, sodium, potassium, magnesium and iron. It is similar in composition to colostrum. Chemical analysis of this secretion in Genser's case gave the following quantities per litre: 5.57 Gm. casein; 4.90 Gm. albumin; 9.56 Gm. milk-sugar; 14.56 Gm. fat; 8.26 Gm. inorganic salts. Microscopically are found milk globules, leucocytes and so-called colostrum corpuscles which, according to Czerny, are milk globules laden with leucocytes, or according to others with epithelial cells. The secretion of milk persists usually into the 11th month. It is said that this secretion may be kept up for a very long time by regularly emptying the gland of its contents. This secretion of the mammary gland in the newborn must be regarded as a physiological process. Whereas former

theories sought to explain this secretion on the ground of a fatty metamorphosis of the central cells of the fœtal "anlage" of the gland, which is solid (Kölliker), or with a desquamation of the glandular epithelium (Epstein), we at present believe that the same stimulation which calls forth the development of the mammary gland in the mother operates on the mammary gland of the fœtus and produces the same reaction (Knöpfelmacher). According to J. Halban this agent is a secretion of the placenta and moreover of the epithelium of the chorion. The secretion passes into the maternal blood and then into the fœtal circulation and causes the development of the lacteal gland. This explanation however does not cover the fact that the secretion of milk does not start until the fœtus has been born. At birth the mammary gland of the newborn shows similar changes to that of the mother; proliferated, feebly staining epithelium, dilated ducts, and surrounding the ducts, hæmorrhages, leucocytes, eosinophiles and giant cells. Shortly after birth the so-called "puerperal involution" (Halban) commences, which operates upon the breast of the child in the same way as it does upon that of a non-nursing mother. The excitation of the milk secretion after birth, which probably depends upon the same cause in both mother and child, is supposed to be due to a cessation of the placental action. A ferment secreted by the placenta inhibits the secretion; its cessation, as the result of the birth, is followed by secretion. Schein assumes a hyperæmia of the gland to be responsible for this. This explanation, however, does not seem to be satisfactory and we must say that the cause for the excitation of the milk secretion is not yet clearly established.

II. MASTITIS IN THE NEWBORN

Inflammation of the mammary gland nearly always occurs in a functionating organ. Hence, acute inflammations of the breast sometimes occur in the newborn just as in women in the puerperium and during lactation. In the child the disease occurs only from the 1st to the 3rd week of life. At the beginning of the attack the breast becomes tender and gradually becomes reddened, and the skin over it œdematous. The vicinity of the gland protrudes as a whole and gradually suppurative softening takes place followed by spontaneous rupture, unless opened surgically. The disease is often accompanied by very high fever, restlessness, anorexia, vomiting and liquid stools. Mastitis must be attributed to infection by micro-organisms; according to Lange, bacteria are present physiologically in the lacteal ducts of the newborn (just as has been demonstrated in adult women). Through trauma these organisms, which are harmless as long as the epithelium is intact, wander into the tissues and set up their inflammatory reaction. Ulcers and fissures of the nipple are possibly also portals of entry for these bacteria.

The **diagnosis** is easily made. It is hardly possible to mistake it for physiological lactation and retention of the secretion, since with the latter, œdema, redness and tenderness are wanting.

The **prognosis** is good; complications such as extensive phlegmonous cellulitis with resultant sepsis are very rare and preventible by rational treatment. The gland is partially destroyed by inflammatory processes and this is of importance for the female, since women who have gone through attacks of mastitis as children, later, in their puerperium, have poorly developed breasts, unsuitable for nursing.

Prophylaxis and Treatment.—To prevent the occurrence of mastitis, the breast of the newborn infant should be protected from all manner of trauma. For this reason expressing the contents of the gland is unqualifiedly interdicted and the secreting gland should be protected from pressure by the application of sterile cotton buffers. With the appearance of the first symptoms of inflammation a dressing should be applied. Gauze compresses soaked in liquor alumini acetatis (P. G.) diluted 8–10 times or in half-strength aqua plumbi, or in 50 per cent. alcohol, are applied to the diseased breast, covered with oiled-silk and fixed by means of a binder.

If fluctuation is demonstrable, incision is indicated. The incision should be made as near the periphery of the gland and as small as possible, and to insure the cutting of the fewest number of ducts, it should run in a radiating direction from the nipple. After incision the wound should be dressed with dermatol or airol, and sterile gauze or possibly with moist dressings. Recovery follows in a few days. It is possible that the application of the suction apparatus, according to Bier, will have a favorable effect in cases of mastitis of the newborn, just as has been shown for the same disease in mothers.

III. VAGINAL HÆMORRHAGE IN THE NEWBORN

In certain otherwise healthy girls there occurs on the fifth or sixth day and sometimes later, a hæmorrhage, usually very scant, from the vagina. Schukowsky found 35 such cases among 10,000 newborn girls. Blood-stained mucus or small blood-clots are found on the labia of the infant; on separating the labia it is seen that the blood comes from the vagina since small clots and strings of blood-stained mucus adhere to the visible portion of the vagina as also to the hymen. In case the hæmorrhage assumes somewhat greater proportions, blood-clots mixed with mucus and clumps of blood-stained mucus are also found in the diaper. The bleeding is never severe enough to come in drops.

In many cases the bleeding stops in a day or two, in other cases it persists for a week or recurs after the pause of a day. The bleeding never disturbs the well-being of the child; the fatal cases of vaginal hæmorrhage reported by Doleris must have been due to other causes.

Inasmuch as they were attended by severe constitutional disturbances, they may have been due to sepsis.

This vaginal bleeding of the newborn cannot be confused with *precocious menstruation* which sometimes occurs with an abnormally early development of the sexual organs. For the genuine premature menstrual bleeding (menstruatio præcox) does not occur in the first weeks of life, but later; moreover it almost always starts after months or years and at least recurs for a few months more or less regularly at monthly intervals; whereas the condition described as vaginal hæmorrhage never recurs. Besides, this precocious menstruation is accompanied by a premature development of all of the sexual organs, the ovaries, mammæ, pubic hair, etc.

In rare cases girls both smaller and larger, have irregularly recurring hæmorrhages from the vagina, which are due to malignant neoplasms. Therefore the vagina must be carefully inspected in every case of vaginal hæmorrhage; polypoid sarcoma of the vagina which produces no other symptoms at its beginning, may thus be discovered.

The **cause** of vaginal hæmorrhage of the newborn was inexplicable until recently. Asphyxia and endometritis have been advanced as the etiological factor in a few cases. Ritter attributed the genital hæmorrhages of newborn girls to the same causes which produce hæmorrhages in other parts of the body. Diseases of the newborn, namely, septicæmia (pyæmia) are so often accompanied by bleedings that the vaginal bleeding of the newborn might also be attributed to the same cause, the genital hæmorrhages being considered as local manifestations of an existing hæmophilic diathesis. Ritter concluded this from his series, which embraced 7 cases of genital hæmorrhage; in 4 of these, hæmorrhage of other organs (gastro-intestinal) was also present.

Later investigations show that Ritter's opinion is not correct. In the vast majority of children with vaginal hæmorrhage, septicæmia is not even to be considered. Still one must admit that according to Ritter's observation vaginal hæmorrhage may at times accompany septicæmia. This is to be considered exceptional; for as a rule healthy children are affected.

Zappert's investigations showed that only hyperæmia and diapedesis of red corpuscles from the dilated vessels take place in the uterus and that signs of inflammation are wanting. This finding is in accord with Halban's investigations according to which newborn girls, with few exceptions, show changes in the uterus which correspond to those found in the premenstrual or menstrual condition of the uterus in the adult; these are: congestion and subepithelial hæmorrhages, sometimes also hæmorrhages into the cavity of the uterus. These changes are called forth in the sexually mature women by a function of the ovaries; in the fœtus and newborn, whose ovaries are functionally undeveloped, the

menstrual changes in the uterus are brought about by substances, circulating in the maternal and fœtal blood during pregnancy, which arise in the placenta, probably in the chorionic epithelium (Halban). Soon after birth the mucosa of the uterus returns to its normal state and the uterus itself becomes smaller; 3 weeks post partum the puerperal involution of the womb is completed (Halban). The changes occurring in the prostates of newborn boys (hyperæmia, hæmorrhages, infiltrations around the glands, secretion) described by Schlachta, are also classified under the reactions of pregnancy which disappear within the first 2–3 months and are attributed to the same cause as the manifestations in the uterus of newborn girls (Halban). The œdema of the vulva which is seen so commonly in newborn girls could also with probability be attributed to the active circulating substances of pregnancy.

This œdema shows itself immediately after birth or in the first days of life and gradually disappears. After this the labia majora are wrinkled or thrown into folds. Similarly an œdema of the penis and scrotum occurs in newborn boys which disappears after days or weeks and is entirely meaningless. These œdemas have been attributed by various authors, to stasis during parturition or to compression of the veins on account of the intra-uterine position of the extremities. The fact that these œdemas occur also in children delivered by Cæsarean section speaks against the first-given explanation (Halban).

C. ICTERUS NEONATORUM

Symptoms.—Usually before the end of the first or second day of life, less frequently not until the third, fourth or fifth day, and only very exceptionally still later, the skin of the newborn takes on a yellowish tint which usually appears first on the face. The icteric tint spreads rapidly over the trunk and extremities. In many cases, especially in the beginning, the physiological hyperæmia of the skin conceals the yellow color, which then only becomes distinct on pressure of the examining finger. Besides the skin, the sclera as a rule, but not always, is distinctly yellow; here the icterus sometimes is completely concealed by ecchymoses or vascular injection. On "expressing" the blood from the mucosa of the mouth, the yellow color comes out prominently in the anæmic area. The yellow color is usually specially distinct in ulcerative processes in the oral cavity (Bednar's aphthæ, etc.); the secretion of suppurative processes is also colored yellow.

The *pulse rate* in the newborn is not influenced by icterus.

The *icterus of older children* is also usually unaccompanied by a slowing of the pulse rate. This must be attributed to the fact that the bile of children contains only small quantities of the biliary acids. Jakubowitsch in an analysis of the bile of children found glycocholic but no taurocholic acid.

The *liver* and *spleen* show no changes. After the passage of the meconium, the feces take on the "yolk-yellow" or green color, characteristic for the nursling. The *urine* is also pale during the course of the icterus. The examination for bile-pigment, with the customary tests, is usually negative. Epstein, alone, claims to have often found bile-pigment in icterus neonatorum by using Huppert's test; and, according to Cruse, bilirubin may be demonstrated in the extract after agitating the urine with chloroform. Halberstam was also able to demonstrate biliary acids, in fact glycocholic acid, in the urine of icteric newborns.

The microscopic examination of the urine during the period of icterus shows clumps of a dark pigment; these were already known to Virchow, were termed "masses jaunes" by Parrot and Robin and were identified with bilirubin by Cruse; the low solvent power of the urine for bilirubin (the urine of the newborn contains usually only traces of the alkaline phosphates which could dissolve the bilirubin) is the reason for the failure of solution of the bile-pigment, which is then usually found forming clumps with epithelial cells for a nucleus.

Icterus neonatorum is usually very slight in degree; at times it is quite intense. The duration of the jaundice varies from two days to three weeks; the intensity of the discoloration determines this. In the majority of children the icterus disappears or becomes indistinct in from six to eight days. In case the icterus increases in intensity toward the end of the second or even the third week, we may well assume that we are not dealing with that variety of icterus termed icterus neonatorum, but rather with an icterus due to some other and usually more serious disease. This disease, in most cases, is *sepsis*, in the clinical picture of which icterus plays a prominent rôle. In case sepsis can be excluded and if toward the end of the first month of life the icterus becomes more pronounced, consideration must be directed toward the possible presence of an obstructive jaundice. The latter condition is, in general, rare in the newborn and may be due to various causes, one of which is a *congenital obliteration of the bile-ducts*, with which condition the feces are only slightly colored and the icterus increases in intensity from day to day until the skin takes on a yellowish green color.

In cases of obstructive or of septic icterus, one is usually able to demonstrate bile-pigment in solution in the urine; this ability to put bile-pigment in solution evidently depends upon changes in the metabolism, which are brought about by the disease and which change the composition of the urine. A positive finding with Gmelin's test or with any other test for bile-pigment, cannot be employed for the purpose of excluding icterus neonatorum, since in the latter disease the reaction is also, at times, positive.

Occurrence.—Icterus neonatorum occurs, with few exceptions, in all children, with varying intensity. Reports vary widely concerning

its frequency; thus Seux declares that 15 per cent., and Bouchut 33⅓ per cent. of all newborn children have icterus, whereas, according to Poruk 79.9 per cent., according to Cruse 84.4 per cent. and according to Breschet all newborn children become icteric. My own observations are most nearly in accord with those of Cruse. The icterus is especially pronounced in premature children, just as, in general, the body weight and the intensity of the icterus are inversely proportional (Cruse). The icterus is said to be especially intense in the children that show shortly after birth a pronounced congestion of the skin. Children in whom the umbilical cord is tied early are said to have icterus less often than those in whom the cord is not tied till the cessation of its pulsations. The children of primiparæ are said to become more intensely icteric than children of multiparæ (Kehrer).

Pathological Anatomy.—Post-mortem examinations in cases of icterus neonatorum are to some extent rendered less conclusive, because it is always some complication which has lead to the fatal termination. Among the findings which must be ascribed to icterus neonatorum, the observation that the liver is often not especially yellow or else only in spots, deserves first mention. This, however, applies also to other forms of icterus. The finding of bilirubin crystals in the kidneys (Meckel, Virchow's hæmatoidin-infarct) is peculiar; these are found in the form of bunches of needles or rhombic platelets, in the tips of the papillæ. Orth found these crystals in every case of icterus neonatorum and moreover not only in the kidneys but also in the blood, in the adipose tissues, the brain and other organs. In examining the cadavers of still-born infants, or those of children dying shortly after birth, Neumann found bilirubin crystals in the fat cells of the peritoneum and in the afferent blood vessels. The precipitation of bilirubin in the fatty tissue may be due to the withdrawal, by the fatty acids in the fat cells, of the alkali, which is the solvent for bilirubin.

For the rest, one finds, at autopsy, a yellow discoloration of most of the internal organs; this is especially marked in the serous membranes, the intima of the vessels, in exudates and transudates and is not noticeable in the spleen or kidneys.

Pathogenesis.—The causes of icterus neonatorum have not yet been clearly established. It can be said that the views concerning the pathogenesis of icterus neonatorum are, in general, parallel to the theories of icterus in the adult and to those of experimental icterus.

If we accept the dictum of Stadelmann "without a liver no icterus," then all theories which seek to explain icterus without involvement of the liver must be discarded. We know from the celebrated experiments of Naunyn and Minkowski that the liver is not only the organ for the excretion of the bile but also for its elaboration. In the liver arise the characteristic components of the bile, the bile-pigment as

well as the biliary acids. It is true that occasionally bilirubin arises, without involvement of the liver, from the blood-pigment, (*e.g.*, in hæmorrhages into the tissues) but icterus has never been observed in this connection. The forms of icterus in which biliary acids are demonstrated in the urine must unqualifiedly be attributed to the resorption of bile in the liver. This presence of the biliary acids has been demonstrated for icterus neonatorum and moreover not only in the urine (Halberstam) but also, earlier, in the pericardial fluid (Birch-Hirschfeld and Hofmeister).

Therefore, all theories which have sought to explain icterus, by means of a hyperæmia of the skin, capillary hæmorrhage and the like, have only a historical interest. Just as little do those theories deserve consideration, which would attribute the icterus to hæmolysis and transformation of blood-pigment to bile-pigment within the circulatory apparatus (hæmatogenous jaundice, Neumann, Violet, and others). The finding of biliary acid in the urine absolutely excludes such a theory. However, one theory, that of Luincke, which explains icterus without liver, is not demolished by this fact; according to Luincke, the biliary components are resorbed from the meconium; since, however, the biliary acids and pigments are normally excreted in the liver during their passage through the portal circulation and therefore do not enter the general circulation, Luincke assumes that a portion of the blood in the mesenteric veins, laden with the biliary constituents of the meconium, passing through the as yet unclosed ductus Arantii, enters the vena cava ascendens and thus into the general circulation without passing through the liver. Against this theory it must be noted that, according to Meckel, the ductus Arantii in the newborn is usually hardly passable by a sound, further that meconium is acid in reaction, whereas bilirubin is soluble in alkaline fluids and finally that the expulsion of the meconium during parturition, for example with asphyxia, does not hinder the occurrence of icterus. We must, therefore, look to the liver as the place of origin for icterus. The most satisfactory theory would be one that would connect icterus neonatorum with a demonstrable stasis of bile. To this end, Peter Franck assumed a closure of the ductus choledochus by means of the meconium; Virchow, by means of a plug of mucus; and Cruse, through cast off epithelium; but these assumptions do not accord with the facts; no more is the theory of Birch-Hirschfeld right, according to which an œdema of the capsule of Glisson is the cause of the stasis; the œdema which Birch-Hirschfeld found was not verified by other investigators and must be attributed to complications (pneumonia, etc.). By anatomical examinations of the liver, Bouchut's hypothesis of a hepatitis and Epstein's theory of a catarrh of the finer gall-ducts have been demolished. The assumption of Ritter and Epstein that icterus of the newborn is, in the majority of instances, of a

septic nature, seems, in the light of clinical observation, untenable; the well-being of icteric children and the absence of any other symptoms of sepsis speak against any such assumption.

Endeavor has been made to attribute icterus neonatorum, in accord with the extensive experiments of Stadelmann, Affanassiew, Tarchanoff and others, to a polycholia or more correctly a pleochromia, which arises as the result of the destruction of countless erythrocytes during the first days after birth (Hofmeier, Silbermann, and others). However, the supposition that during the first days of life there is an extensive disintegration of red cells has been refuted and with this refutation the hypothesis of a pleochroic icterus becomes untenable.

Investigations have shown that the blood of the newborn is, at birth, richer in corpuscles and hæmoglobin than that of the adult. A count of six to seven million erythrocytes in a cubic millimetre is not uncommon. This count sometimes increases, during the first two or three days of life and then falls (Lepine, Hayem, and others). The explanation of this has already been given by these writers. The increase and decrease in the number of cells is only apparent and is brought about by variations in the quantity of the blood plasma. Cohnstein and Zuntz furnished the experimental proof.

In nursling animals showing variations in the number of cells per cubic millimetre, similar to those of newborn children during the first days of life, determinations of the total number of red cells have indicated that their number increases from the first day of life but never decreases. Microscopic examination and the determinations of the resistence of the red cells have shown, contrary to Silbermann, the absence of the products of red cell destruction (Fischl, Knöpfelmacher).

The destruction of red cells in the newborn has also been connected with the "physiological transfusion" which every newborn experiences at birth. At birth a large part of the blood present in the placenta is expressed into the fœtus; and when the cord is tied off late, this amount is further increased (according to Budin by about 90 Gm. or 3 oz). This superfluous blood is said to be destroyed during the first days. Hofmeier endeavored to verify this hypothesis by metabolism experiments. As far as the erythrocytes are concerned, it has been established that they are not destroyed in abnormal numbers.

Two other peculiar theories rest on the assumption of a destruction of blood corpuscles in the newborn. Silbermann advanced the one: the destruction of the erythrocytes is supposed to lead to "fermentæmia," through this to capillary stasis and thromboses in the liver, and thus to icterus. Such thromboses, however, have never been found, not even by Silbermann himself. With this, Silbermann's theory also falls.

Recently Leuret has affirmed anew the destruction of red cells in

the newborn. It is supposed to occur in consequence of the cooling of the skin after birth. Through this, as in paroxysmal hæmoglobinuria, there arises a hæmoglobinæmia. Leuret found this but no one else has. The hæmoglobin in the circulation is changed, in the tissues, to a yellow coloring matter. Since, however, a hæmoglobinæmia does not exist in the newborn, the hypothesis of Leuret must also be rejected.

Endeavor has also been made to connect the icterus with a post partum fall in the blood pressure (Frerichs). This assumption, however falls, since icterus is especially intense in asphyctic children and those with pulmonary atelectases; and in these affections the blood pressure is increased.

Not more fortunate is the assumption of a compression of the gall-ducts by the dilated liver veins, distended in consequence of the aforementioned transfusion. Histologic examination of the liver in the newborn shows the gall-capillaries not compressed but on the contrary much dilated (Abramow); my own observations have also taught me this fact. In preparations in which the bile-capillaries are demonstrated according to the method of Eppinger, one sees them mostly varicose and tortuous, as an expression of the extreme fulness of the gall-duct system; and moreover this is present immediately after birth and in those still-born.

In reconsidering the remarks concerning these various theories, we are forced to the conclusion that up to the present time no single theory is fully compatible with the facts. Icterus neonatorum in this respect resembles the icterus occurring with infectious diseases and with sepsis in which, similarly, the anatomical examination of the liver gives no explanation of the resorption of bile.

In order to make the passage of the bile over into the blood comprehensible, in such cases, one can assume with Minkowski, Liebermeister and others, that we are dealing with a functional secretory anomaly of the liver cells; according to Minkowski, in such cases the liver cell has lost the faculty of sending the bile-pigment and biliary acids into the gall-ducts alone and gives these substances up to the blood-capillaries also. According to Pick, the bile is directed into the lymphatic system. According to Abramow, an increased secretion of bile gives rise to this secretory disturbance; the liver cell produces bile profusely but its excretory energy is not able to overcome the abnormally high pressure in the bile-capillaries and consequently the bile is turned into the blood-capillaries by the cell. The overloading of the blood-capillaries, the passive congestion, are the causes for the assumed functional disturbance of the liver cell, which Abramow terms "asthenic polycholia."

It is my belief that the causes of icterus neonatorum lie in the overfilling of the bile-capillaries in the fœtus, with rather tenacious bile, and

in the lively production of bile by the liver cell immediately after birth, in consequence of the rich supply of blood. The newly-formed bile cannot flow out through the over-filled bile capillaries and, therefore, passes from the liver cell into the blood-capillaries. Accordingly, icterus neonatorum is a *physiological manifestation.* It offers the most favorable prognosis and leads to no complications. The statement that it exerts an effect on the general health of the child, has not yet been substantiated. It has been stated (Schaeffer) that intensely icteric children especially lose weight during the first days of life. It is possible that a considerable resorption of bile and biliary acids can be held responsible for this.

Medical intervention in cases of icterus neonatorum is in no sense indicated.

III. DISEASES OF THE NAVEL

A. ANATOMICAL AND PHYSIOLOGICAL INTRODUCTION

At birth the umbilical cord forms the connecting link between the body of the embryo and the placenta. It is a cord, about as thick as the little finger, twisted in many spirals and consists fundamentally of the jelly of Wharton, an embryonic mucous tissue which contains countless connective tissue and elastic fibres embedded in its colloid matrix. The cord is covered with amnion throughout its length; this terminates abruptly about 1 cm. above the fœtal abdominal wall, leaving the proximal portion covered with skin. The umbilical cord contains no capillaries; only at its point of entrance into the navel does there appear, in the peritoneal tissue, a rich capillary network, whose branches extend on to the intra-abdominal portion of the umbilical vessels and send numerous twigs upward into the collar of skin covering the lowest portion of the cord; here, at the boundary between amnion and skin, they form a vascular circle (Hyrtl).

At birth the umbilical cord contains:

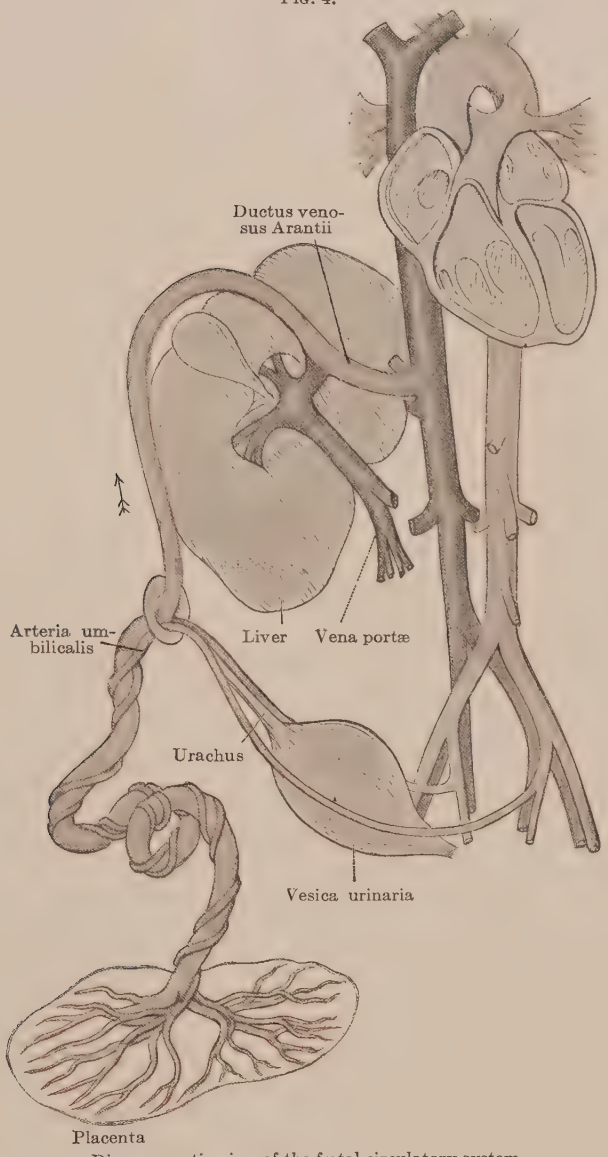
1. The two umbilical arteries which conduct the blood from the fœtal body to the placenta. They extend to the navel on either side from the common iliac artery; they are thick walled vessels and like the umbilical cord, are wound in spirals.

2. The umbilical vein which conducts the blood from the placenta to the inferior vena cava. It passes through the cord to the body of the child, thence through the navel ring along the abdominal wall to the left branch of the portal vein which conducts the placental blood through the ductus venosus Arantii into the inferior vena cava of the fœtus.

3. Strands and epithelial remains representing a portion of the *ductus omphalomesentericus* (the vitelline duct), which disappears at the first month of fœtal life.

4. Clumps of cells arising from the involuted *allantoic duct.* The extra-abdominal portion of the allantois undergoes retrograde metamorphosis in the first weeks of fœtal life; leaving only a few epithelial

FIG. 4.



Diagrammatic view of the fœtal circulatory system.

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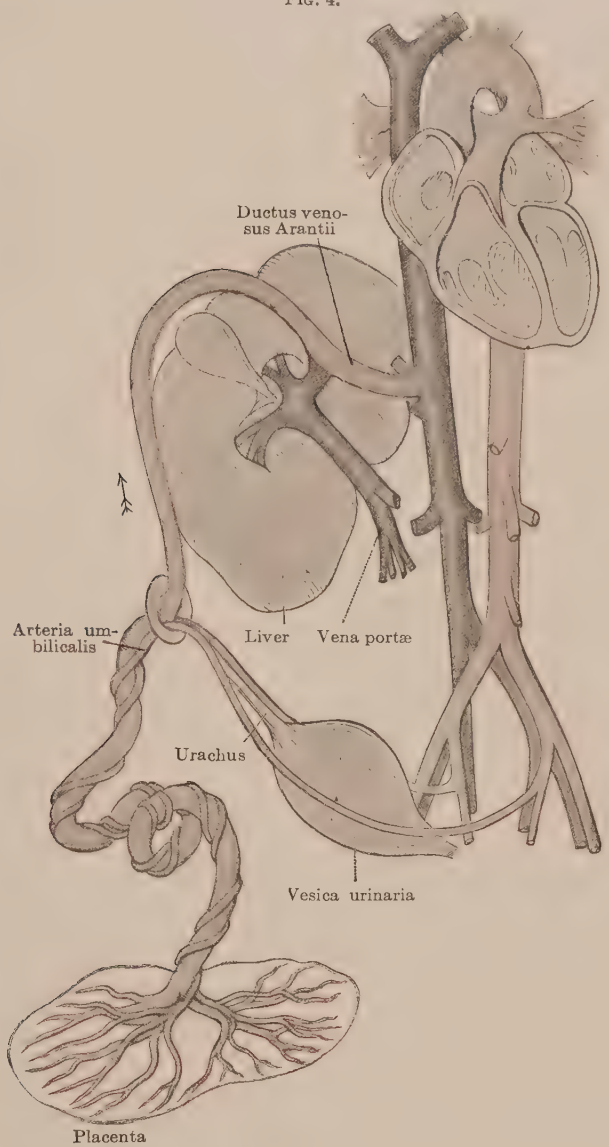

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Immediately after birth, usually after the cessation of pulsations in the umbilical arteries, the cord is cut; among civilized peoples, after

previous ligature. There remains adhering to the body of the child a portion of the cord, one or more centimetres in length, which undergoes mummification during the first days of life. On the fourth to ninth day, rarely earlier or later, it separates from its attachment with a slight inflammatory reaction. The separation occurs later with thick œdematous cords and in premature children than with thin cords and strong children. The skin of the abdominal wall which covers the beginning of the cord for a distance of 1–1½ cm., rolls in at the same time and thus forms the umbilical fold, the upper half of which is smaller than the lower. The navel fold usually hides the base of the navel so completely that one is unable to see its epidermization without separating the folds. The healing of the navel wound progresses, with scant secretion, by epidermization from the periphery toward the centre.

The healing of the navel wound and its pathological disturbances depend closely on the peculiar construction of the umbilical vessels. The umbilical arteries differ materially in structure from the other vessels of the body. They possess a single layer of endothelium and a highly developed musculature. The latter is arranged in two layers. The inner layer is composed of longitudinally disposed fibres richly mingled with elastic fibres and connective tissue. The outer layer is still thicker, contains principally circular fibres and is poor in elastic substance and connective tissue; occasionally besides the circular fibres it contains some longitudinal fibres. Further, the umbilical arteries are enveloped in a dense mantle of embryonic connective tissue; this forms the adventitia of the arteries and accompanies them downwards through the navel ring into the abdominal cavity as far as the summit of the bladder.

Examination of the lumen of the *umbilical artery* in the constricted state shows it to be very narrow and in the form of the letter Y; this comes from the inward bulging of the vessel walls as a result of the contraction of its longitudinal fibres; this contraction almost completely closes the lumen of the vessel, an open lumen being found for only short distances. This, however, only holds good for the umbilical arteries of children born viable, whereas these bulgings never occur in the arteries of still-born infants. The *umbilical vein* forms a smooth wide tube and possesses likewise a single layer of endothelium; its musculature runs in various directions but is for the most part circularly disposed. There is a band of elastic fibres beneath the endothelium (Bondi); the muscular coat is traversed by wavy connective tissue and by a few elastic fibres. In its extra-abdominal portion the umbilical vein also possesses a well developed adventitia of embryonic connective tissue, which is wanting in its abdominal portion, where the vessel lies rather free in its surroundings (Herzog).

At the moment of birth as a consequence of the opening of the pulmonary circulation the blood pressure in the aorta and in the entire

greater circulation, including the umbilical arteries, falls; for now, instead of both sides of the heart, only the left side is active in pumping the blood through the systemic circulation. The umbilical arteries gradually contract throughout their extent; the contraction commences in the peripheral portion and extends to the abdominal portion and is materially assisted by the mechanical irritation arising from the cutting of the cord and perhaps also by its cooling; thus the arteries are so well contracted that in the vast majority of cases no bleeding takes place after the cutting of the cord even should no ligature be applied. The vein also contracts; its contained blood flows out, and under normal conditions shortly after birth it is either empty or contains only a thin clot in the neighborhood of the navel. Since the cord, as stated, possesses no blood vessels of its own for its nourishment its death begins with the cessation of the placental circulation. This occurs normally through a process of *mummification,* which is assisted by all factors promoting evaporation, especially by warmth and dry air.

The dessication begins at various points on the cord and is as a rule completed by the third day. Then the cord is converted into a dark, ropy, flat body; the drying out process takes place throughout the cord except at its base and here the cord stays moist over a few millimetres of its extent and disintegrates gradually. Simultaneously changes occur in the navel, corresponding to a demarcating inflammatory process; these cause the separation of the cord. The cylinder of skin which covers the lower part of the cord swells and becomes red; its border frees itself slightly from the cord and begins to roll in upon itself; in this way there is formed between the cylinder of skin and the dessicated cord, a furrow which is filled with greasy material composed of tissue detritus, pus cells, and bacteria. On histological examination the capillaries of the network under the skin covering the cord are widened and collections of leucocytes are found in the skin and in the jelly of Wharton. The cord gradually loosens at its base, remaining longest attached at the blood vessels. Occasionally the stumps of the vessels protrude several millimetres out of the base of the wound after the cord has separated. Meanwhile the infolding of the skin-cylinder progresses gradually and after the separation of the cord, the small skin wound, usually covered with a secretion or crust, lies in a little funnel. At the same time epidermization starts at the periphery and becomes complete about three weeks after birth.

Shortly after birth the process of involution begins in the abdominal portion of the umbilical vessels. The peripheral portions, at the navel itself, become involved in the inflammatory processes taking place at the navel; their walls are invaded by round cells and their lumina closed by small-celled infiltration. The thrombi, which are regularly found in the arteries seldom form in the veins. The intima prolif-

erates and gradually becomes converted into connective tissue (arteritis obliterans). In the third week of life degeneration of the media occurs; the muscularis seems shredded and is permeated with capillaries, its structure becomes indistinct and the nuclei stain feebly; later the muscular coat disappears, being replaced by connective tissue. The veins and arteries usually remain passable for a thin sound for months and occasionally for years after birth.

The adventitia of the umbilical arteries furnishes the material for the formation of a dense connective tissue and this attaches the arteries, as well as the connective tissue strands resulting from their involution, to the navel ring and to its lower half. Thus the lower half of the ring is closed by a strong buttress of connective tissue, the fibres of which extend into the skin of the navel. Conditions are however different in the upper half of the navel ring. Only a few loose strands of connective tissue form around the umbilical vein. The vein, after its fibrous metamorphosis, draws over to the connective tissue bolster which is formed from the adventitia of the arteries and thus there ensues a defect in the upper half of the navel, between the upper half of the ring and the connective tissue strands of the vein which are drawn over to the arteries; this defect is covered underneath, toward the abdomen, by only the thinnest of connective tissue layers and thus offers a place of lessened resistance against the impact of the abdominal contents on crying or straining. Herzog designates this defect the "canalis umbilicalis."

Some writers teach that the media and intima of the umbilical vessels retract, so that in the upper portion, lying nearest the navel, only the adventitia changed into connective tissue, remains attached. This retraction, however, is disputed by well-known authorities (Herzog, Kockel).

After its involution the navel appears as a defect in the abdominal wall, closed by connective tissue tightly in its lower half, insufficiently in its upper portion. The *fascia umbilicalis* (the portion of the transversalis fascia lying underneath the navel) extends beneath the connective tissue and below this is peritoneum. The umbilical vessels are changed to tense fibrous bands. From the vein, the ligamentum teres is formed, passing along the anterior abdominal wall in the free margin of the falciform ligament of the liver until it reaches the median incisure. That part, alone, of the umbilical vein which connects with the left branch of the portal vein normally remains patent, and persists as a branch of the portal vein, being traversed by the blood in a opposite direction to that in fœtal life.

The umbilical arteries, after their obliteration and conversion into connective tissue, form the lateral umbilical ligaments, which extend from the lateral pelvic wall to the anterior abdominal wall and running properitoneally pass to the umbilicus.

B. CONGENITAL ANOMALIES OF THE UMBILICAL REGION

(See Plate 7)

1. *Amniotic Navel.*—Normally the skin of the abdominal wall extends for about 1 cm. over the umbilical cord, the base of which it cylindrically encircles. In very rare cases the skin is lacking over the lower part of the cord and the adjacent abdominal wall, so that the amnion not only extends over the lowest part of the cord but also spreads out over the skin defect as a delicate, transparent membrane.

The navel ring, the fibrous tissue, abdominal muscles and peritoneum are, however, normally developed. The disc of amnion becomes dessicated like the cord, turns dark in color and separates after a few days. The skin-defect heals by granulation and scar-formation. The life and progress of the child are not influenced by this anomaly.

2. *Cutis Navel.*—(Skin navel, cutaneous umbilicus).—A not uncommon anomaly occurs when the abdominal skin is not drawn in like a funnel, after the separation of the cord, and thus the formation of the navel-folds is wanting. Then there appears in the umbilical region a projecting cylinder of skin, about 1–1½ cm. in length, at the apex of which the umbilical wound is found. The wound heals and the skin cylinder persists. This anomaly has been explained by assuming that the abdominal skin extends for an abnormally great distance over the cord (Widerhofer). However, it is more probable that in a large number of instances, the cutis navel does not arise in this way, but rather because of the failure of the physiologic infolding of the free margin of the skin of the cord, which should follow the separation of the cord. Umbilical hernia occurs frequently in such children. With the growth of the child the superfluous skin of the umbilicus is drawn upon for the covering of the abdomen so that it gradually disappears completely.

3. *Hernia of the Umbilical Cord.*—(Congenital umbilical hernia; hernia funiculi umbilicalis).—In the sixth to tenth week of fœtal life the umbilical cord contains one or more loops of intestine, which later in fœtal life are drawn back into the abdominal cavity. The persistence of intestinal coils and other abdominal organs outside of the body cavity constitutes a failure of development which should here be considered on account of its frequency and the good results achieved by proper surgical treatment.

Symptoms and Course.—The umbilical region in the newborn is found occupied by a swelling which is half-globular, egg-shaped, or pear-shaped. Its size varies; tumors from the size of a nut to that of a child's head have been found. They have a bluish-white transparent covering which is continuous with that of the cord; the cord is not usually attached to the middle of the tumor but rather to its lower half. The covering of the mass is sharply defined from the abdominal skin

which surrounds its base. If the covering is transparent one is able to recognize the intestinal coils or the other abdominal organs. The covering is, however, usually thickened in spots and sometimes in its entirety. The delicate transparent covering is formed by the amnion and the parietal peritoneum. The thickened areas result from the spreading of Wharton's jelly over the covering of the tumor and sometimes from fibrous thickening following an inflammatory process. On palpation, the tumor is of a soft consistency containing harder masses within. It is sometimes attached to the abdomen by a broad base and sometimes it has a pedicle. If the child lives a few hours or days, the covering becomes opaque and inflammatory signs ensue at the border of the abdominal skin; soon the covering of the mass dries up at the same time as the cord and then it separates. In very rare cases (and especially

Fig. 5.

Hernia of the umbilical cord containing the liver and intestines.

where the rupture is small) the hernial contents may return into the abdominal cavity; the abdominal cavity is then closed by granulations and thus the hernia is cured; or else the exposed parts, after separation of the tumor covering, become, as a consequence of an active inflammation, covered with granulations which gradually undergo epidermization and the healing of the hernia is thus brought about. These are, however, very rare occurrences. In the vast majority of instances peritonitis occurs after the separation of the hernial sac or before, and death follows.

With very large herniæ, or in difficult deliveries, the sac sometimes ruptures during labor and the child is born with extruded viscera. In some cases gangrene of the intestines and the formation of a fæcal fistula occur even within the first days; in such cases the accompanying peritonitis results fatally.

Pathogenesis.—The occurrence of hernia of the cord is generally

attributed (Oken, Ahlfeldt) to the failure of the intestinal coils, normally present in the cord in the second and third fœtal months, to return to the abdominal cavity before its complete closure. The cause of this lies, according to Ahlfeldt, in the behavior of the ductus omphaloentericus, the vitelline duct, which in the second fœtal month extends from the yolk-sac through the cord to the intestinal tube. Normally this duct becomes thinner and thinner and finally atrophies completely. The intestinal coils leave the cord and fall back into the abdominal cavity before the abdominal wall closes down to the opening necessary for the passage of the structures of the cord. However, the return is hindered in those cases where the ductus omphalomesentericus either does not disappear at all or else where it does not disappear until the cavity is closed down to the umbilical ring, the opening for the vessels of the cord and the urachus. It is difficult to explain the origin of those herniæ in which the liver, with or without the intestine, forms the hernial contents.

Ahlfeldt's explanation might suffice, in the cases where the liver and other organs, together with intestines lie in the amniotic covering; on account of the extrusion of the intestinal coils there is more room in the abdomen for the other organs; these are, therefore, less tightly held in place, become more movable and fall into the hernial sac. Possibly the prolapse of the liver has some connection with the excessive growth of this organ and especially of its left lobe (Tandler).

According to Aschoff one can not explain these herniæ, nor herniæ of the liver alone, nor any umbilical cord herniæ, by a persistence of the ductus omphalomesentericus; but rather in a totally different way. Aschoff assumes that in these cases the liver is not developed laterally in the abdomen under the closed abdominal wall, as in the normal development; but rather in an abnormal location. The abnormal position of the umbilical veins in these cases argues for this theory. This explanation may be considered as satisfactory for the rare cases in which the liver alone is found in the hernial sac.

The **prognosis** of hernia funiculi umbilicalis was formerly an absolutely unfavorable one. However, since the institution of the operative treatment, the prospect of the survival of the child is very promising, if the operation is performed as early as possible. According to the statistics of Kindt, out of 65 cases treated by operation, 50 were cured.

The **treatment** of hernia of the cord must not be expectant. Before the introduction of asepsis, operation was shunned and the treatment consisted in covering the sac with gauze; with small herniæ the contents were sometimes reduced and the hernial sac closed with plaster or by applying silver coins. At the present time we believe that every co-called conservative method should be discarded and as soon after birth as possible one of the operations recommended should be per-

formed. The so-called radical operation, first performed by Lindfors in 1882, is the simplest; the hernial sac is opened and cut away, the skin margins are freshened and after reposition of the hernial contents the abdominal wound is sutured. Amniotic adhesions must be loosened. Olshausen recommends an extraperitoneal method in which the amnion is separated from the peritoneum and the latter with the hernial contents is replaced without opening the peritoneal cavity; the edges of the opening are then freshened and sewed together. In the cases in which reposition without opening the sac can be carried out, or where the contents are very small, C. Breus recommends the employment of *percutaneous ligature*. The organs are replaced, a clamp is placed around the sac, taking in the skin, and the sac is then opened and dissected away; below the clamp two or more sutures are passed through and through and knotted and the clamp removed.

4. *Persistence of the Ductus Omphalomesentericus* (Vitelline Duct). —Physiologically the omphalo-enteric duct which leads from the yolk-sac to the intestinal tube, is obliterated by the end of the second fœtal month. In case obliteration does not occur, various anomalies can arise, the most important of which, for the newborn, is the open Meckel's diverticulum. In such cases the ductus omphalo-entericus is patent in its abdominal portion and sometimes for a short distance in the cord. After the cord separates, the wound does not heal completely and there remains a narrow, constantly secreting fistula. In marked cases the fistula is wide open, persistently discharging a cloudy fluid, easily identified as intestinal contents. In other cases, fluid may be obtained by passing a small soft catheter; examination, chemical and microscopic, of this fluid shows it to be intestinal contents (fat globules, acidity, odor, negative murexide test).

In other cases the umbilical wound heals over, but a short time later some secretion appears. In these cases epithelial adhesions close the peripheral end of the duct and later gradually loosen. In other cases a tumor about the size of a hazel-nut with velvety surface is found in the navel region either immediately after the separation of the cord or else a few days or weeks later; this shows a prolapse of the wall of the fistula and in rare cases a prolapse of intestinal coils through the fistula can occur. Cases of umbilical fistulæ in which the walls show a structure similar to the gastric mucosa are totally obscure.

The **diagnosis** of an open Meckel's diverticulum is as a rule not difficult. It is important not to confuse the small tumor resulting from prolapse of the mucosa of the diverticulum, with a sarcomphalus or an enteroteratoma. It can be differentiated from patent urachus fistulæ by a chemical and microscopic examination of the secretion.

The **prognosis** is very good. Rational therapy demands the excision of the whole diverticulum by laparotomy. However, conservative

treatment by cauterizing the fistula with silver nitrate or the actual cautery, sometimes effects the closure of the fistula.

5. *Urachus Fistulæ.*—The stalk of the allantois, which extends to the summit of the bladder, becomes obliterated in its extra-abdominal portion during the second fœtal month. Its abdominal portion persists as the urachus and its lumen is either totally or partially obliterated.

Fig. 6.

Persistence of the ductus omphalomesentericus. Prolapsed Meckel's diverticulum.

In exceptional instances when there is obstruction to the outflow of urine through the urethra, a condition occurring more often in boys than in girls, the urachus remains patent throughout, forming a fistulous tract which terminates at the umbilicus. After the separation of the cord one finds, at the umbilicus, a fistula from which urine is passed, either upon pressure or during micturition.

In some cases, just as with a patent Meckel's diverticulum, a small,

tender, red tumor is found in the umbilical region, varying in size and bearing the fistulous opening on its summit. The tumor owes its origin to a prolapse of the mucosa lining the urachus. Probing and the chemical examination of the evacuated fluid for uric acid, as well as its microscopic examination, confirm the diagnosis.

The **treatment** consists in the cauterization of the fistulous opening. Should this not avail, suture of the walls of the fistula, after freshening their surface, is recommended.

C. DISEASES OF THE NAVEL

1. Affections of the umbilical cord sometimes occur while the cord is still attached to the child. *Moist gangrene* (sphacelus) occurs very commonly. Instead of mummification progressing steadily, the stump of the cord, either wholly or in its central part alone, becomes discolored, swollen, foul smelling and a brownish secretion soaks through the dressings. Occasionally a small mummified portion remains behind after the separation of the cord; and the stumps of the umbilical vessels are sometimes seen sticking up through the ragged remains of the cord. In the course of a few days this tissue is cast off by means of a serous or seropurulent inflammatory demarcation. These disturbances of the separation of the cord are often accompanied by slight fever, a symptom easily understood, since bacteria thrive in the stump of the cord even under normal conditions.

All procedures which inhibit the normal dessication of the cord further the development of its diseases. Moist heat plays the most prominent rôle in this connection. It has been maintained, but not at all accepted, that the daily bath of the infant exerts a retarding effect on the dessication of the cord.

The **prognosis** of these disturbances is, in general, favorable, although the infection occasionally spreads and can then lead to any one of the various diseases of the umbilicus itself. Prophylactically the strictest asepsis in the care of the cord and the avoidance of oily or moist dressings are enjoined.

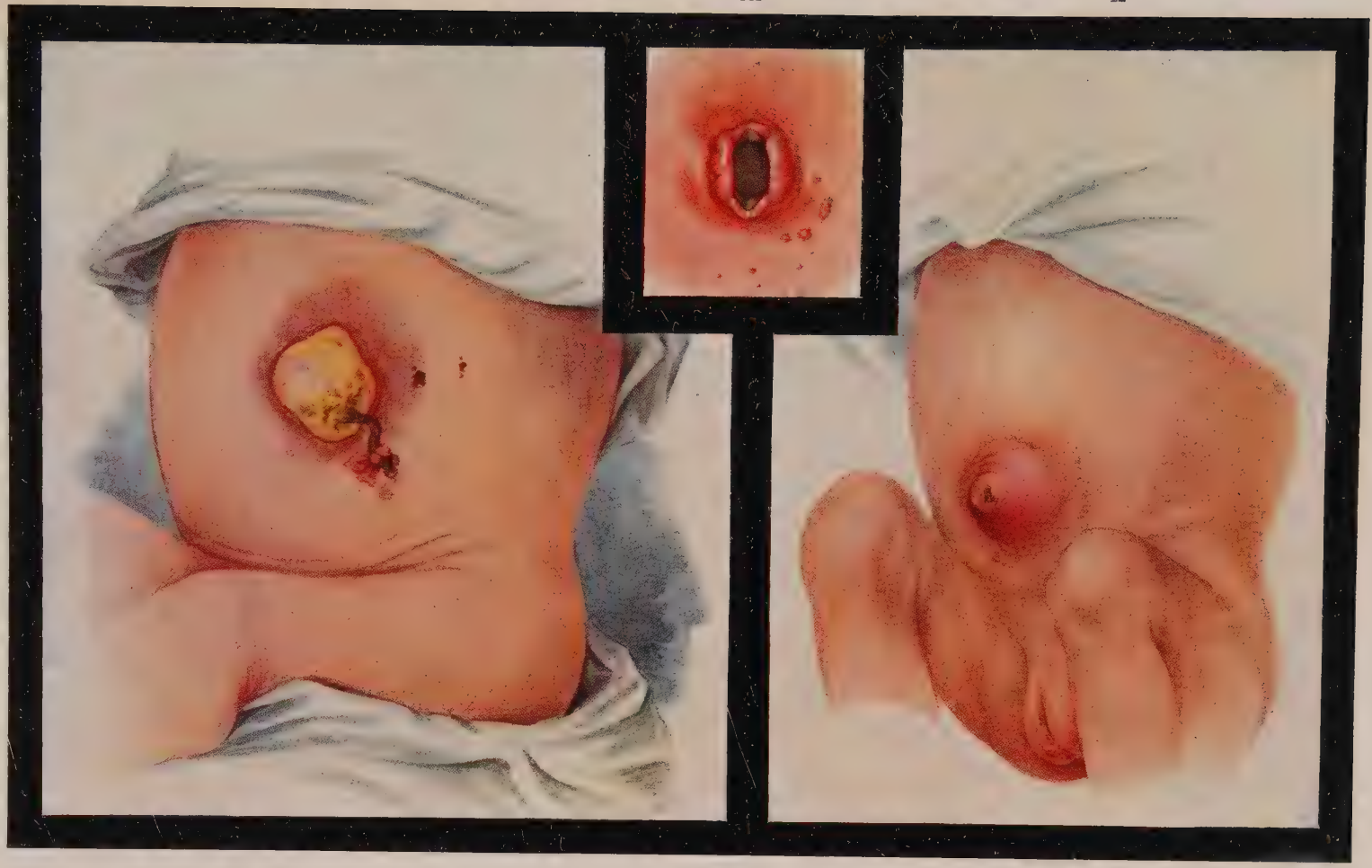
The **treatment** consists in removal of the infected cord, preferably by thermo- or galvano-cautery, and the application of antiseptic powders.

2. After the cord separates, a serous or seropurulent discharge sometimes arises and persists for several days; this secretion is usually caused by some infectious agent but in rare instances may be the result of mechanical or chemical irritation. The umbilical fold is either normal in appearance or becomes slightly reddened and at times œdematous; after wiping away the discharge flabby granulations are seen at the base of the as yet unhealed navel wound. This condition has been termed *catarrhal omphalitis, excoriatio umbilici* or *blennorrhœa umbilici.*

The **diagnosis** should be made only when the other conditions

PLATE 7.

I III II



I. Amnion navel. II. Omphalitis. III. Umbilical ulcer, after separation of swollen navel folds.

which give rise to the more refractory discharges from the navel can be excluded, such as diseases of the umbilical vessels; fungus, ulcers and umbilical gangrene.

The **prognosis** is very good, since the condition heals in a very few days. The treatment requires the use of antiseptic dusting powders (dermatol, xeroform, airol, and salicylic acid) or pencilling with silver nitrate (1–2 per cent.) or peroxide of hydrogen (2–3 per cent.); the application of a 1–2 per cent. borated vaseline dressing or a moist dressing with liquor alum. acet. (P. G.), diluted 8 times in water or aqua plumbi (P. G.), diluted 2–3 times.

3. *Umbilical Ulcer.*—Suppurative processes as a result of infection, can arise from ulcerations in the umbilical wound. In this case the umbilical folds are œdematous, covered with crusts or a purulent secretion and sometimes also reddened. On separating the navel folds a smeary gray or gray-green exudate appears, which in some cases can be easily wiped off, but in others is fibrinous and adherent. After removing the exudate the ulcer readily comes to view. The ulcers occasionally extend to the cutaneous covering of the navel and then attain considerable proportions (see illustration); however they usually are only about the size of a pea. The stump of the umbilical artery can often be seen at the bottom of the ulcer, as the arterial wall offers a greater resistence to the necrotic process than do the other tissues; the perivascular tissue is always involved in the inflammatory process.

Umbilical ulcers are, as a rule, caused by infection with one of the well-known bacteria of inflammation. In rare cases, however, a fibrinous exudate is the sign of true diphtheria, the confirmation of which lies in a bacteriological examination.

The **diagnosis** of ulcer is made by inspection.

The **prognosis** is good; extensive tissue destruction is to be feared only in marantic children.

In case the ordinary antiseptic wound treatment does not avail, the **treatment** consists in cauterization either with silver nitrate or with the thermo- or galvano-cautery (Escherich).

4. *Acute Umbilical Cellulitis* (Omphalitis).—In rare cases, shortly after the separation of the cord, while there is still some discharge from the navel wound, there occurs a reddening and œdema of the navel fold, rapidly spreading to the surrounding skin of the abdominal wall for several centimetres and extending downwards even to the pubes. The superficial veins of the abdominal wall are regularly congested and at times the inflamed lymphatics are seen as stripes extending from the navel.

Pus wells up from the bottom of the umbilicus unless prevented by crusts. The navel often protrudes conically and the skin of the navel fold and vicinity becomes shiny by reason of the tense œdema;

sometimes the whole neighborhood takes on a bluish tint in consequence of the venous stasis.

Fever, restlessness, excessive whimpering, distention of the abdomen and anorexia are present. The legs are often flexed on the abdomen. This condition consists in an inflammation of the subcutaneous tissues of the umbilical region.

In many cases abscesses form; in a smaller number gradual retrogression of the inflammatory signs take place and in rare instances complications like gangrene, arteritis, phlebitis and peritonitis occur. One case reported by Widerhofer led to the formation of an intestinal fistula. Acute umbilical cellulitis has its origin in infection of the umbilical wound and, therefore, the navel itself is involved, usually the seat of an ulcer covered with a lardy, fibrinous exudate.

The **diagnosis** is easily made by reason of the tense œdema and redness.

The **treatment** consists in moist compresses of liquor alum. acet. (P. G.), diluted about eight times, or aqua plumbi (P. G.), diluted twice, together with the opening, along a grooved director, of any abscesses that may be present.

5. *Umbilical Arteritis and Phlebitis.*—Infections of the umbilical cord and umbilical wound very often lead to diseases of the navel region, which spread along the umbilical vessels.

These infections can spread in two ways. In the first place they may attack Wharton's jelly, the sheath of the umbilical vessels, which extends around the arteries and the vein, and for a short distance inside the abdomen; then the infection spreads downwards by way of the lymphatics; so that there exists a periarteritis or periphlebitis and from this vascular disease and infection of the thrombi in the vessels can arise. The second way is by direct infection of the vessels and then we have a primary arteritis or phlebitis. The second way is, at least for the artery, the less frequent, the disease usually beginning as a periarteritis.

Infection of the arteries and their adventitia (for the jelly of Wharton is thus to be considered), is much more frequent and also much more benign than infection of the vein. This long disputed observation, advanced by Bednar and by Widerhofer, stands as valid.

Individual cases of arteritis and periarteritis show marked *variations in their course.* In some cases the disease runs its course without symptoms and can go on to recovery without having given any sign of its existence. Umbilical arteritis and periarteritis can involve either the entire length of the vessel or only a portion of it. In cases where only a portion of the vessel is involved, no local symptoms occur unless the peripheral portion of the vessel is affected as far as the navel. In such cases the navel wound is covered with crusts or else a little pus

oozes out of the navel ring or can be squeezed out by stroking the abdominal wall from the symphysis toward the umbilicus. Careful inspection will occasionally reveal a small fistulous opening, often passable for a thin probe (with great care on account of the danger of hæmorrhage in case the sound enter the lumen of the vessel and dislodge a clot). The probe takes a direction toward the sacrum and can pass for a considerable distance downwards; this manœuvre should always be executed without any force. It has been shown that the probe usually penetrates the necrotic periarterial tissue. However, in other instances of circumscribed umbilical arteritis and periarteritis, the peripheral part of the vessel is perfectly normal and the navel shows no visible changes; but a portion of the vessel wall, at a distance from the end, is diseased. Inflammatory processes, with or without abscess formation, arise; the existence of these inflammations is sometimes manifested only by a slight fever, in the majority of cases, however, they run their course without giving rise to any symptoms, or they may be suspected because of failure to increase in weight or of a loss in weight or conditions of collapse in the child, otherwise inexplicable. It may be helpful, then, for diagnostic purposes, to palpate if possible the thickened, cord-like navel arteries, as hard resistances through the abdominal wall. In these cases abscesses form between the peritoneum and the abdominal muscles and extend to the peritoneum and also toward the scrotum, where, burrowing in the subcutaneous cellular tissue they may reach down to the thigh.

In the severest cases of periarteritis and arteritis, the whole vessel is diseased and then, besides the suppuration at the navel (which, however, may heal very quickly) there may occur frequent, though slight, rises of temperature, distention of the abdomen, dyspeptic symptoms from the gastro-intestinal tract, not uncommonly purulent peritonitis umbilical hæmorrhages (Bednar) and also septicæmia with all of its severe symptoms, as they will be described in the following section. Besides peritonitis, purulent or serous pleurisy, pneumonia, subcutaneous abscesses, phlegmons, periostitis, osteomyelitis, infarcts in the spleen and kidneys, nephritis, purulent meningitis, cerebral hæmorrhages, and encephalitis may result.

In accord with the researches of Basch and the observations of Finkelstein we are justified in assuming that arteritis and periarteritis as a rule remain local and only lead to systemic infection in a small percentage of cases.

Doubtless, however, the existence of umbilical arteritis through toxæmia, lowers the resistance of the child and thus renders him more susceptible to other maladies, such as gastro-intestinal affections and pneumonia, although these latter are not necessarily to be considered as evidence of a general septic infection. For this assumption, the identifi-

cation of the organisms in the lungs with those in the umbilical vessels is wanting, as is also their demonstration in the blood. The few investigations of this nature conducted by Finkelstein gave negative results. It is important to know that infection of the umbilical vessels can, and in most instances does exist without any visible change in the umbilicus itself. It is just the very severe infections that are especially prone to occur while the umbilical cord is still attached to the umbilicus. There is sometimes, then, a delay in the separation of the cord and sometimes the cord shows slight signs of putrefaction. After separation of the cord, infection of the vessels or their sheaths can occur primarily without involvement of the navel or secondarily by extension from a local disease of the umbilicus. The possibility cannot be excluded, however, that umbilical periarteritis can in occasional very rare instances occur as a secondary local manifestation of septicæmia arising from some other cause.

An infection of the umbilical vessels may occur any time after the first day of life as long as the navel wound has not completely healed; according to Buhl it can be acquired even in utero or during the passage through the birth canal. The infection of the navel probably occurs ordinarily from the fingers of the nurse or physician, possibly through the bath or dressings.

The frequent coincidence of umbilical disease and ophthalmia suggests the possibility of the infection being carried from the conjunctival pus to the cord (Runge). Contamination of the umbilical wound with infected lochial secretion also deserves mention.

The *micro-organisms* to be considered as causing arteritis and periarteritis are: staphylococcus pyogenes aureus and albus, bacterium coli, streptococci, bacillus pyocyaneus and the diplococcus pneumoniæ.

The disease occasionally occurs epidemically in maternities (Wassermann: pyocyaneus infections).

The *duration* of arteritis and periarteritis varies from a few days to several weeks. Premature children are remarkably prone to affections of the umbilical vessels.

The *autopsy findings* in severe cases of arteritis and periarteritis show extensive inflammatory lesions in the vessels and perivascular tissues,—in the latter alone, in a few early cases. The pathological changes involve either the entire vessel, or only a portion of it, or only the perivascular tissues. Correspondingly we find the umbilical arteries, which are usually involved on both sides, thickened and cord-like; the vessels are either symmetrically dilated or sacculated; on cross-section the walls appear considerably thickened, œdematous, infiltrated, the intima lustreless and damaged in spots, and the surface of the vessel uneven. In the lumen there are sometimes cheesy masses, sometimes pus with or without blood-clots. In severe cases the changes due to

septicæmia or caused by a complicating disease are never lacking. Not even in the severest cases can the changes in the vessels be traced as far as the retroperitoneal tissue. In other cases the intima is not appreciably changed and the vessel contains no pus, but the perivascular tissue is necrotic over a large area and converted into a large pus cavity with or without an external fistula.

The **prognosis** of the disease is, in general, not unfavorable; cases running a prolonged course, however, terminate fatally from sepsis, peritonitis, or sometimes from a complicating pneumonia or nutritional disorder.

Umbilical phlebitis and *periphlebitis* are encountered considerably less often than arteritis and most frequently in feeble children. The arteries are surrounded by a much stronger, circular layer of connective tissue (Runge) which accompanies them for a distance of a few centimetres inside the abdomen and this furnishes a good culture medium for infections. But there is only a scanty layer of Wharton's jelly around the vein and this extends for only a short distance. The rarity of umbilical phlebitis depends upon these anatomical relations; moreover, it is usually accompanied by an arteritis. In a large number of cases, umbilical phlebitis gives rise to no local signs at the umbilicus. Thus the dictum of Porak and Durante seems justified, that the severest cases of umbilical infection show the slightest local signs. The existence of a phlebitis can only be assumed clinically, from the various general symptoms of septicæmia to which the phlebitis regularly leads. According to Bednar, pus cannot be expressed from the vein in uncomplicated cases; in such cases diagnostic importance must be ascribed to a gradual daily increase in the intensity of the icterus up to a dark discoloration of the skin (ictère bronzé, Porak and Durante), possibly also to an oozing of blood from the navel while in the process of healing. Other signs of sepsis, namely, those on the serous membranes, are likewise usually not primary in the newborn, but secondary, and may then have diagnostic value.

Sometimes such *complications* as erysipelas, umbilical gangrene, etc., arise, and expedite the fatal outcome, which practically always supervenes.

At *autopsy* one often finds pus in the vein, sometimes only a thick coagulum which fills the greatly dilated vein (this of itself is pathological), and is infected by bacteria (Porak and Durante); sometimes diffuse hepatitis or else multiple abscesses in the liver; œdema or inflammation of the capsule of Glisson; very often peritonitis; and other signs of sepsis.

Whereas the **prognosis** of umbilical arteritis umbilicalis is comparatively favorable, that of umbilical phlebitis is very unfavorable, as the malady is almost inevitably fatal.

The **prophylaxis** of all navel affections demands strict asepsis in the care of the navel and the employment of methods which favor the mummification of the cord.

The **treatment** of this group of umbilical diseases avails practically but little; surgical intervention can only be recommended when there are circumscribed abscesses in the first portion of the artery or in the periarterial tissue. Otherwise we limit ourselves to the employment of antiseptic umbilical dressings with antiseptic powders or wet dressings with liquor alum. acet. (P. G.), diluted 8–10 times. These may be applied with the "apron dressing" of Flick, which Escherich recommends. Stimulants must be given in conditions of collapse and with complications the appropriate local or symptomatic treatment must be instituted.

6. *Umbilical Gangrene.*—Since the recognition of asepsis gangrene of the navel, which was formerly very frequent, has become one of the rarest diseases, occurring only in feeble or poorly nourished children in the first weeks of life (according to Bednar exceptionally as late as the 9th week). It usually follows an omphalitis or some other local navel affection; more rarely, in atrophic children, it occurs without any demonstrable local disease. The destructive process involves the navel in a circular area of greater or less extent, sometimes with and sometimes without the formation of blebs; it next attacks the muscular layers, causes peritonitis and sometimes leads to perforation of the peritoneum and extrusion of the viscera. In very rare cases necrosis of the wall of an intestinal coil, lying adjacent in front, occurs, with the formation of an artificial anus; then intestinal contents are discharged from the navel; in case the intestinal coil adjacent does not become at first adherent, a diffuse peritonitis will arise as a result of infection of the peritoneum by feces. Erosion of the umbilical vessels and severe hæmorrhage are also among the dangers of this malady. In cases of extensive gangrene, collapse with or without fever and death in coma usually occur. The few cases (according to Fürth, 15 per cent.) in which recovery has been observed, soon show a cessation of the necrosis; round about the gangrenous area a reactive inflammation goes on, granulations are formed and healing takes place.

The **treatment** by using the thermo- or electro-cautery far into the healthy tissue (as with noma), might possibly avail in the beginning of the disease; this procedure should not be carried out in very atrophic children. Otherwise, antiseptic powders, cauterizing with nitrate of silver and warm baths have been recommended.

7. *Umbilical Fungus.*—(Sarcomphalus, umbilical granuloma).—As early as the second or third week of life, a tumor may form within the navel fold as the result of the failure of the navel wound to heal and of the consequent abnormal proliferation of the granulations. This tumor,

at times flat and sessile and at times pedunculated, is attached to the base of the navel wound, is fleshy in color, has an irregular raspberry-like surface and gradually attains the size of a pea or even a hazel-nut. At times the tumor is hidden by the folds of the navel and can be seen only when the folds are held apart.

In case these formations are left to themselves, an eczema of the skin of the navel fold arises as a result of the persistent secretion; the tumor persists for weeks and even months, but finally shrinks gradually and becomes covered with skin. In adult life one occasionally finds in the umbilicus, little projections covered with skin, representing the remains of such fungi.

The *histological examination* of these tumors reveals in the vast majority of cases a highly vascular granulation tissue (Küstner); in a number of cases, however, the tumor is composed of glandular tubules, lined with cylindrical epithelium, or else of smooth-muscle and connective tissue. These neoplasms are then known as enteroteratomata (Kolaczek) or adenomata (Küstner) and owe their origin to partial prolapse of the imperfectly involuted omphalo mesenteric (vitelline) duct (Kolaczek), or else to a proliferation of cells, epithelial in nature, which are left behind in the granulation tissue at the time of the separation of the cord (v. Hüttenbrenner). In a few cases the last-mentioned author found cuboid epithelial cells (rests from the urachus) which had subsequently proliferated.

The **diagnosis** is easily made. One must only bear in mind the possibility of patent urachus-fistula with a protuberant mucosa or a persistent patent vitelline duct, the peripheral end of which is somewhat prolapsed. In the latter case intestinal contents issue from a fistula which admits the passage of a probe for a considerable distance. Moreover these latter swellings have a tumor-like, smooth surface and are not uneven and irregular. Since the sarcomphalus does not heal spontaneously or else very slowly, it should be touched with lunar caustic to hasten its involution. In other cases it can be tied off with silk, which insures its separation after 2–3 days or it can be cut off with the scissors, after ligature. All these manipulations are painless since the sarcomphalus contains no nerve-endings.

Other tumors of the umbilical region are extremely rare. Angiomata, myxosarcomata and cystomata have been reported.

8. *Umbilical Hæmorrhages.*—Hæmorrhages from the navel may be divided into three classes. The first group comprises the cases in which bleeding occurs, only *from the arteries*, shortly or only a few hours after birth, despite the ligation of the umbilical vessels. This hæmorrhage comes from the cut surface of the cord and occurs occasionally immediately following its ligation and cutting. This can occur only under two conditions: first, when the ligature is not sufficiently secure; and

second, when the physiological cessation of the circulation in the umbilical arteries does not take place. Shortly after birth the umbilical arteries are normally no longer filled by the blood current, since they are shunted out of the arterial circulation as a result of the expansion of the lungs and the fall in blood pressure. Moreover, the ligation of the cord is followed by contraction of the muscular coat of the umbilical arteries and closure of the vessels.

The umbilical artery is well adapted for this powerful closure by reason of the peculiar arrangement of its musculature, as described in a previous chapter (Preliminary Physiological Remarks). Normally, therefore, ligation of the cord would be supererogatory. However there are children in whom the fall of the blood pressure fails to take place and in whom death from hæmorrhage might occur, should the cord not be ligated. To this category belong the asphyctic newborn infants; or those whose lungs have only partially expanded; especially also, premature children; also those who for other reasons have been partially asphyxiated and finally children in whom abnormal conditions of the blood pressure prevail on account of disturbances of the circulation (congenital heart disease). E. Hofmann calls attention to the fact that suffocation itself causes a rise in the arterial pressure which would facilitate umbilical hæmorrhage.

In some cases the bleeding does not occur immediately after the cutting of the cord but follows some hours later. In these cases the ligature is applied correctly but as a result of the drying up and shrinkage of the cord the band becomes loose and, if the vessels have not contracted, they bleed. The above-mentioned forms must be designated umbilical cord hæmorrhages in contradistinction to the following.

The second group comprises those rare cases in which the hæmorrhage occurs *from the lumen of the umbilical vessels* (and here moreover it is exclusively the arteries and not the veins which bleed) *at the level* of the umbilicus. Ritter, who was able to report 97 cases of umbilical hæmorrhage saw this bleeding from the vessels only seven times. The blood came in spurts in one case only; in the others in small drops. In Grandidier's collection of 202 cases there are only 7 cases of bleeding from the vessels, and among these, two cases in which the blood spurted from the vessels.

This hæmorrhage occurs within the first days of life (according to Ritter, at the latest on the 15th day). The cord has always separated or else is in the process of separation, since it clings longest to the arteries and these (or only one of them) must be separated before a hæmorrhage from the vessel can occur at the level of the umbilicus. In connection with this, the normal closure of the intra-abdominal portion of the navel vessels must have failed.

The *parenchymatous umbilical hæmorrhages* which form the third group are relatively the most frequent. With this condition, although the umbilical vessels are closed, the blood trickles "just as from a sponge" from the small vessels and from the capillaries at the base of the navel, both before and after the separation of the cord. This bleeding usually occurs in the first or second week of life and only in rare cases and then in poorly nourished infants, does it come on later (Ritter reports one case occurring on the 63rd day of life). The bleeding either takes place continuously or interruptedly, it lasts many hours and even days and leads to serious loss of blood which often causes the death of the child. According to Grandidier only 17 per cent. of these children recover. This depends only partly on the fact that the children bleed to death, in part, however, the children die of the underlying constitutional disease.

Parenchymatous umbilical hæmorrhage, like hæmorrhage from the umbilical vessels, is in the majority of cases the result of a demonstrable sepsis and is often (but not always) accompanied by symptoms of that disease. Hæmorrhages from other organs and from parts other than the navel often occur with this condition, and, not seldom, local diseases of the navel [arteritis-phlebitis, umbilical gangrene (Ritter)].

In other cases umbilical hæmorrhage is referable to hereditary syphilitic disease of the vessels. This must be admitted as etiologically of moment (reference to this subject will be found in the chapter on Melæna), since Bondi only recently has again described specific changes in the blood vessels due to hereditary syphilis.

It does not seem to have been demonstrated that umbilical hæmorrhage ever occurred as the result of hæmophilia. One finds, however, in Grandidier's tables a few cases of such hæmorrhage occurring in children whose mothers belong to hæmophilic families, but in these cases other cases of navel bleeding do not seem to be excluded. (The etiology of local hæmorrhage in the newborn receives consideration in the chapter on Melæna.) We do not consider as pathological the slight bleeding which takes place on the days immediately following the separation of the cord or which occurs from the mechanical irritation of the granulations (*e.g.* from the examination by the physician or from rubbing with cotton, etc.). Occasionally traces of blood or small crusts are then found on the navel dressings.

Therapy.—Hæmorrhage from the cord may be controlled by energetic ligation, possibly with heavy silk or with rubber bands (drainage tube) (Budin). After separation of the cord the bleeding can be stopped by applications of adrenalin solution, or ferric chloride or calcium phosphate and compression and, finally, by suture of the umbilicus. Should one have to deal with the rare instance of a genuine bleeder (hæmophilia) or with a child whose blood has a greatly impaired capacity for clotting,

in which case, as with the septic disease, the blood oozes from the needle-holes, the hæmorrhage must be controlled by continuous compression. In all cases of umbilical hæmorrhage which cannot be controlled by agents applied locally, the use of subcutaneous injections of gelatine (Merck's, absolutely sterile), in the dose of 10–20 c.c., (2 to 6 drams) is recommended.

9. *Umbilical Hernia.*—(Navel ring hernia, hernia umbilicalis).—Protrusion of the abdominal contents through the navel ring occurs with great frequency in childhood and usually in the first months of life. The navel ring, especially in its upper section, is closed only by a few strands of connective tissue. The place which corresponds to the passage of the umbilical vein through the navel ring and which is called the umbilical canal by Herzog (see anatomical introduction) easily gives way to the intestinal pressure occurring when the child cries and strains; the fascia and peritoneum are pushed forward, the intestines enter and gradually widen the aperture, thus causing ruptures from the size of a pea up to that of a prune. Schmidt assumes that a pit-like depression must be found in the peritoneum by the time the navel heals in order for a hernia to develop.

Symptoms.—When the child lies quietly a loose pocket of skin can be seen in the navel region. When the hernia is small, it is covered with normal skin and when larger with thinned-out skin. At its summit or a little below, is the thinned out navel scar. When the child strains or cries, the intestinal contents are pressed forward into the sac, and they can be reduced with a gurgling sound. Then the sharply defined opening of the hernial orifice which is usually round, can be felt; its circumference is formed by the navel ring. The hernial sac consists of the peritoneal protrusion and the fascia umbilicalis, while the small intestine and rarely the omentum form its contents.

Course and Prognosis.—Umbilical herniæ in nurslings heal spontaneously in the majority of instances. Healing in infancy fails in only a small number of cases and then the probability of healing decreases from year to year. Umbilical herniæ not healed within the first 3–4 years remain open for life unless treated by operation. In some cases adhesions between the sac and contents occur but strangulation occurs very rarely.

Prophylaxis and Treatment.—Inasmuch as umbilical herniæ occur in a very large number of nurslings during the first months of life, it is incumbent upon the physician to examine the umbilical wound carefully, and if there be the slightest sign of a stretching of the scar and especially if the baby cries a great deal or strains as the result of constipation, it is well, after the third week of life, to apply an umbilical bandage, as a prophylactic. The wearing of a navel binder is futile.

Adhesive straps answer this purpose best. Two or three strips of

adhesive plaster, 2–3½ cm. (¾–1½ in.) wide, and about 12 cm. (5 in.) long, are used; the skin in the navel region is drawn, by the mother or an assistant, over the navel into two parallel linear folds, forming an elastic cushion over the hernial orifice; the straps are tightly applied overlapping one another and thus effectually hold this cushion down. Instead of the three strips, one strip about 50 cm. (20 in.) long can be used, passing it around the body and crossing it over the skin-folds held by the mother or assistant. Many physicians recommend the use of a flat disc, for example a gold piece, fastened over the hernial orifice with adhesive plaster. The adhesive should be, as far as possible, non-irritating and should be changed at least once a week. The treatment should be interrupted if necessary until the subsidence of any eczema that may arise from the irritation of the strips.

If healing of the hernia does not take place within the first year, the further use of the adhesive bandage is usually without avail and then recourse must be had to spring or elastic trusses.

Escherich recently recommended, in such cases, the introduction of an intraperitoneal paraffine disk. For this purpose the child is anæsthetized and by means of a special syringe, a few c.c. of paraffine (melting point 39° C.; 102° F.), are injected, into the hernial sac, previously emptied of its contents by lateral compression. The paraffine is then hardened by means of an ether spray directed by an assistant, and is molded by pressure into the form of a disk. The point of puncture is covered with sterile gauze and an adhesive dressing applied as in the conservative treatment. In other cases, those in older children, and where the hernial orifice is larger, an operation, consisting of the extraperitoneal reposition of the hernial sac and contents, is necessary. Ventral hernia can be prevented by dissecting the recti from their sheaths and sewing their edges together.

IV. INFECTIOUS DISEASES OF THE NEWBORN

A. TETANUS NEONATORUM

Tetanus neonatorum is classed with the wound infections of the newborn, just as erysipelas of the newborn, because its port of infection is regularly the umbilical wound. Tetanus in the newborn runs a similar course to that in the adult and differs in no wise from the latter in etiology or symptomatology. The healing of the navel wound is usually complete in about 14 days and this implies that tetanus neonatorum is limited to the first three weeks of life, except when the virus gains entrance elsewhere than at the navel.

Symptoms.—The disease starts shortly after birth, usually in the second week, less often at the end of the first or during the third week of life. The onset is accompanied by great restlessness and frequent

piercing cries. It soon becomes evident that the child has some difficulty in sucking. When the infant is put to the breast or given the bottle, it makes only one or at the most a few sucking movements and then desists. The examining physician at this time finds a spasm of the muscles of mastication (trismus) which is elicited as often as the child is induced to suck and which later becomes permanent. This tetanic spasm, the principal symptom of the disease, is not, however, long limited to the masseters. Within a few days or even hours the recurring attacks of tonic convulsions spread to the muscles of the face and therewith the face takes on a characteristic appearance (risus sar-

Fig. 7.

Tetanus neonatorum. (Facies tetanica.)

Fig. 8.

Tetanus neonatorum. (Wrinkling of the skin of the face and spasm of the upper extremities.)

donicus, facies tetanica). The forehead is gathered into deep wrinkles, very striking for a child of this age; the eyelids are squeezed together, the puckered mouth is protruded more or less; at times the corners of the mouth are drawn sharply downwards, in other cases the upper lip alone is contracted or else to a greater degree than the lower lip, thus drawing the skin here into radiating folds. The spasm next extends to the muscles of the neck and back; the head is strongly retroflexed, opisthotonos begins, the abdominal walls become rigidly contracted, the upper extremities usually rigidly flexed to an acute angle and the legs extended. The hands are usually flexed in all joints and the feet

held in dorsal flexion. The position of the extremities varies according to the muscle group which is most intensely affected by the tetanic convulsions.

At this stage on account of the spasm of the masseters and the muscles of deglutition, sucking and swallowing become impossible. Not uncommonly tonic spasms of the larynx and diaphragm occur. Emitting no sounds, the child lies prostrate, becomes cyanotic and breathes irregularly and superficially. The attacks become more frequent and of longer duration so that they seem to be almost uninterrupted. They are aggravated by external stimuli. Touching the skin, taking hold of the nipple, or cooling the body surface by uncovering the child serve to arouse stormy, jerky, tetanic contractions. In many cases the disease runs an afebrile course, in others however it is accompanied by irregular fever which at times is very high. A post-mortem rise in the body temperature has been found very often in cases of tetanus. The complete clinical picture is not always encountered. In many cases the spasms extend no further than the masseters, accompanied by slight contractions of one or the other muscle groups, usually of the face and neck.

Fig. 9.

Tetanus neonatorum.

In the further course of such light cases, the spasms gradually diminish in frequency and intensity and finally cease entirely. Even fully developed cases of tetanus may end in recovery; the spasms diminish gradually, especially the trismus and spasms of deglutition; then the rigidity diminishes, and convulsions occur only after powerful stimuli and later not at all; in such cases I have observed, even after the disappearance of the tonic spasms, a slow contraction of the muscles, elicited by the tap of a hammer, which persisted quite a while.

As a rule, in uncomplicated cases the other organs show nothing noteworthy. It must be noted, however, that septic infection may often accompany tetanus in the newborn. The navel wound presents either nothing abnormal, or else exudes a serous, sero-sanguinolent or purulent secretion. In many cases the umbilical wound has a lardy exudate and has the characteristics of an umbilical ulcer.

Etiology.—Tetanus neonatorum, like tetanus in the adult, is due to a specific agent, the tetanus bacillus. The older opinions which attrib-

uted tetanus to the use of baths of too high temperature, to the influence of drafts, cold, etc., must be regarded as false. Nicolaier in 1885 discovered and cultivated the tetanus bacillus and Kitasato obtained it in pure culture. It is a very constant inhabitant of the ground, in gardens, and has also been found in the dust of dwellings, in cracks in the floors, in furniture, etc., (Bäumler). It gains entrance to the umbilical wound with dust, probably by contamination from the baby-clothes, the bandage, or the hands of the nurse. There may perhaps be an infection of the umbilical cord, just as with sepsis. In the newborn, the bacillus of tetanus was demonstrated by Kitasato, in a case of Baginsky's and later also by Peiper, Bäumler, and others. The bacillus of tetanus multiplies at the seat of infection by spore formation and, except in the rarest instances, does not invade the body; it produces toxins however, which, according to the investigations of H. Meyer and Ransom, are absorbed from the lymph-spaces, for the most part through the ends of the motor nerves, and probably through the axis-cylinders of the motor nerves. These toxins reach the central nervous system, where they become fixed. The combination of these toxins with the motor cells in the anterior horns of the spinal cord and the nuclei in the medulla, gives rise to an abnormal increase in the irritability of these centres and therein lies the cause of the tetanic contractions. The motor centres then react to very insignificant stimuli. The peripheral nerves and the muscles are not involved, as is proven by the cessation of the tetanic spasms after section of the nerve-trunks.

Before the onsent of the tetanus there is an incubation period varying from two days to a few weeks after the infection with the bacillus tetanus. This fact however cannot have any relation to the time needed for the production of a quantity of poison sufficient to produce its effect, but probably depends upon the fact that the passage of the poison through the nerve-trunks requires a certain time before it reaches the motor centres. Others have assumed that the irritation of the motor centres is not due to the toxins *per se*, but to a compound of the toxins and body-substances. These poisonous compounds are supposed to circulate in the blood of the individual infected with tetanus and the blood of such individuals should therefore immediately, without a latent period, produce tetanic spasms in the mouse, an animal especially susceptible to tetanus. In many cases the tetanus toxin also circulates in considerable quantities in the blood of infected individuals. In such cases experimental injection of the toxin-containing blood may produce tetanus. This has not only been established as regards the blood of adults and of animals, but also in one case of tetanus neonatorum.

Even at the very beginning of the disease the tetanus bacillus is still demonstrable in the navel wound in only a small number of the

cases. It probably dies off very quickly. Other septic bacteria are constantly found here.

Escherich recommends curetting the navel wound with a sharp spoon in order to demonstrate the bacillus. The scrapings should be used for the inoculating of mice and making cultures.

Duration and Course.—Tetanus neonatorum runs a very violent course in the majority of cases and cases terminating fatally last only a few days or even hours. In cases ending in recovery the disease runs a more protracted course, extending at times over several weeks. Unfavorable cases terminate as the result of spasm of the diaphragm or less often of exhaustion.

At *autopsy* nothing is found that might be characteristic of death from tetanus. Even the most careful examinations of the central nervous system have up to the present time furnished nothing positive. Whatever hæmorrhages have been found in the spinal cord, brain and other organs, must be attributed to stasis following obstructed respiration.

The **diagnosis** of tetanus is easily made in both the newborn and the adult. It may be confused with the tonic spasms occurring with cerebral disease. Such spasms occur in the newborn in consequence of cerebral and meningeal hæmorrhages and rarely with purulent cerebrospinal meningitis, encephalitis or other cerebral diseases.

The author recently saw a child three weeks old with chronic congenital hydrocephalus in which intermittent tonic spasms occurred, in all the extremities, on moving or handling the child.

Congenital spastic diplegia can give rise to no confusion in diagnosis. In doubtful cases it is advisable to make a bacteriological examination or mouse inoculation. A negative result proves nothing however against the existence of tetanus, and then the attempt can be made to produce tetanus in the mouse by the injection of the toxic blood.

The **prognosis** is in general very unfavorable. It appears to be even worse than with older children and adults. Concerning the frequency of recoveries reports vary, but on the average probably 20–30 per cent. of the cases recover.

Prophylaxis and Therapy.—Since we know that tetanus is an infectious disease, it is our duty to protect the navel wound by the use of aseptic dressings. It also appears that amongst the class of people who lay little stress on cleanliness in the care of wounds, tetanus and also tetanus of the newborn occur relatively with greater frequency. On this fact, moreover, probably depends the reported racial predisposition of certain peoples. When tetanus breaks out in a number of persons, for example in an institution or a neighborhood, it is recommended to use prophylactic inoculations with the tetanus antitoxin discovered by Behring and Kitasato. The tetanus antitoxin is produced by injec-

tions of tetanus toxin in the horse; according to the discoveries of Behring and Kitasato the injection of this toxin causes the appearance, in the blood-serum, of certain bodies which give the serum the ability to prevent tetanus, when introduced subcutaneously into an animal previously inoculated with tetanus toxins or bacilli. In a few species it has also served to cure the disease when already active. The antitoxin operates by combining with the toxin. The bacilli are not influenced, the antitoxin not being bactericidal. The combining of the toxins and the antitoxin takes place both in vitro and in the animal body. In case however large quantities of the toxins are already bound to the nerve-cells, the antitoxin is usually unable to break up these combinations and is therefore only able to neutralize the poisons circulating in the blood. When one remembers that even at the onset of the disease the poisons are combined with the nerve-cells, it becomes evident why the serum therapy of tetanus has not given any convincing results up to the present time. Notwithstanding this, the employment of the serum must be recommended in every case, inasmuch as we never know how much, if any, poison still remains in the peripheral nerves or is possibly circulating in the blood or lymphatic vessels; the poisons circulating in the blood can surely be neutralized. Behring's antitoxin comes in bottles each containing 250 immunizing units (that is, such a quantity of antitoxin as is capable of neutralizing ten times the minimal fatal dose of toxin for a guinea-pig). Besides this there are other reliable preparations on the market. The injection should be given as early as possible; it is recommended to inject one half the dose subcutaneously and the other into the brain (Roux and Borrel) or, more simply, into the subdural space. For this purpose the point which Quincke recommends for lumbar puncture is selected, that is, the space between the spinous processes of the second and third or third and fourth lumbar vertebræ. According to Meyer and Ransom no better result can be expected to follow the subdural than the intravenous injection of the antitoxin. These authors consider injection of the nerve-trunks to be indicated in every case in which the point of entrance of the infection is known and in which the nerves involved, as conductors of the poison, are accessible.

This method of using antitoxin is not, however, available in the newborn. The injection may be repeated, and possibly several times, if no beneficial effects are shown after twenty-four hours. The serum has no deleterious effects; its curative powers, according to what has been said, are uncertain. The injection of brain emulsion, which, according to Wassermann, fixes the tetanus toxin, has given no beneficial results; therefore we must avail ourselves of those *drugs* which are capable of lessening the irritability of the central nervous system. Of these the choice is chloral. It is given in solution, by mouth as long as the child

can swallow and then by rectum, 0.5–2.0 Gm. (8–30 gr.) per day. The bromides and chloroform anæsthesia have as a rule little effect. The use of morphine in effective doses is made difficult by reason of the age. Monti recommends the subcutaneous injection of the fluid extract of physostigma in the dose of 0.006 Gm. ($\frac{1}{10}$ gr.). Others recommend hypodermics of atropine, 0.00001–0.00002 Gm. ($\frac{1}{6000}$–$\frac{1}{3000}$ gr.) per day. Especial care must be taken to protect the child from being disturbed and from cold, inasmuch as all stimuli further the occurrence of the tetanic spasms.

Rest and quiet, enveloping the child in wraps and the use of thermophores are worthy of recommendation. The *nourishment* requires especial attention. As long as the child can suck it is put to the breast. At the very beginning of the disease, however, the child sucks unsatisfactorily, or else not at all. Then it becomes necessary to pump the breast-milk and to feed the infant by using a spoon. With artificially fed children the same procedure is carried out using modified cow's milk. Very soon, however, difficulty arises in feeding the child even by the spoon, since the trismus interferes. The child must then be fed through a catheter passed through the nose into the stomach. For this purpose one employs a thin, soft catheter, about No. 6 English, equipped with a glass tube and with a glass funnel attached to the latter by means of a soft rubber tube. This apparatus must be boiled immediately before each feeding.

B. ERYSIPELAS

Erysipe as is a wound infection, which leads to a rapidly spreading inflammation of the skin and mucous membranes. It arises at times from large wounds and at times from insignificant breaks or excoriations of the skin. In the newborn the infection gains entrance as a rule at the umbilical wound, only very rarely elsewhere and then usually through the skin of the genital organs. Since the vogue of anti- and a-sepsis in obstetrical practice, the occurrence of erysipelas, as of the other wound infections of the newborn, has become much less frequent. Older children are subject to the infection under the same conditions as adults.

Symptoms.—In case erysipelas occurs in a newborn infant the umbilical region, at the end of the first or beginning of the second week, shows a slight redness which spreads quite rapidly downward over the lower part of the abdomen. The affected parts are very œdematous and feel warm; at times pale-red spots are seen in their vicinity. In some of the cases the affected area has a rampart-like boundary which advances with the spreading of the disease. Within a few hours or days the disease advances over the pubic region and the lower extremities. Only in a small percentage of the cases does erysipelas of the newborn

spread upwards to reach the chest, head and upper extremities. (The author observed this only once in ten cases). As a rule the lower part of the body is the first and most severely affected. The disease is not always accompanied by fever. Chills are not observed in the newborn; the fever rises gradually, in many cases is very high, remains high or falls before death; in other cases the disease runs its course without fever. The wall-like boundary and the redness are often not pronounced in the newborn. The œdema, however, is always very marked and tense; it may persist long after the disappearance of the redness and the healing of the erysipelas; then it is gradually absorbed. Blebs are formed in the skin just as with erysipelas in the adult. Not uncommonly the formation of necrotic areas in the skin is seen in cases which last several days; these usually affect the scrotum or the extremities and especially the skin over the small bones or on the dorsum of the foot. In one case observed by the author there was necrosis of the skin of the penis as well as of the scrotum. In such cases circumscribed areas of the skin varying in color from dark-blue to black occur, which, gradually becoming necrotic, form rapidly spreading ulcers with a lardy surface. Phlegmonous processes leading to suppuration are rare.

Virchow saw develop, in the pharynx of a child with erysipelas, an acute phlegmon which caused attacks of suffocation.

Etiology.—The disease is caused by the entrance of streptococci into the skin. We owe the knowledge of this fact to the investigations of Fehleisen. The streptococcus of erysipelas differs in no way, however, from the streptococcus pyogenes. Earlier clinical facts had already supported this, von Eiselsberg produced erysipelas in animals by using streptococci from the pus of phlegmons. Koch and Petruschky furnished the experimental proof that erysipelas in man can be produced by using streptococci cultivated from abscesses. The streptococci enter the lymph-spaces and wander further in them. Infection of the newborn probably takes place from the hands of the midwife, the nurse, possibly also of the physician, through the dressings and clothes. Children of mothers suffering from puerperal diseases are attacked with relatively greater frequency. In this connection the assumption is justified that the infection takes place from the infected lochia of the mother, through a third person or through the dressings.

In one case coming under the author's observation a physician who had dressed a patient with erysipelas assisted at a delivery on the same day. The mother became septic and the child infected with erysipelas on the fifth day. In another case a nursing baby was infected from a purulent mastitis and developed an erysipelas starting on the skin of the lip.

Erysipelas of the newborn is often accompanied by convulsions and somnolence, vomiting and liquid stools. In some cases there are

symptoms of sepsis; inflammatory processes of the navel (arteritis, etc.) are often demonstrable. In occasional cases the abdomen becomes very tense and tender to the touch, the œdema over it being especially pronounced and highly distended veins being visible in the skin of the thorax and upper part of the abdomen. In such cases one must keep in mind the possibility of an acute peritonitis which sometimes (probably as a result of the general septic infection) accompanies erysipelas neonatorum. This complication I have observed in two cases. Erysipelas in older children varies in no way from that in the adult. High fever accompanying it is the rule. Glandular swellings are usually demonstrable. It remains only to call attention to the now rare occurrence of *vaccination erysipelas*. Formerly, in the days of humanized virus, this appeared as veritable epidemics.

Course and Progress.—Erysipelas neonatorum spreads very rapidly, as a rule, and with few exceptions results in death with manifestations of cardiac weakness. In older children the course is usually less violent and recovery takes place much oftener. With them also we not uncommonly encounter relapses and recurrences.

Pathology.—In the diseased areas besides the hyperæmia, an extensive œdema of all the layers of the skin is found with small round-celled infiltration of the skin and subcutaneous tissues. Also lymph-node swellings, enlarged spleen and parenchymatous degeneration of the glandular organs. In many cases in the newborn diseases of the umbilical vessels and sometimes sepsis can be anatomically demonstrated. In uncomplicated cases innumerable foci of streptococci outside of the blood vessels in the affected area may be detected.

Therapy.—The treatment of erysipelas in general, promises no brilliant results. The treatment with antistreptococcus serum as inaugurated by Marmorek, though theoretically well grounded, has completely failed in practice. Attempts to prevent the spreading of the erysipelas, by sealing the affected area and vicinity, have had, in the main, no definite results. For this purpose oil-paints, varnish, shellac, (siccative, Gersuny) and gutta-percha tissue have been recommended. Wölfler applies strips of adhesive plaster at a short distance from the boundary of the affected area, for the purpose of compressing the lymph-spaces and thus furnishing a hindrance for the migration of the streptococci. As a rule moist dressings are employed and compresses of liquor aluminii acet. (P. G.) diluted 8 times, or alcohol 50 per cent., sublimate 1–1000, boracic acid 1–2 per cent., salicylic acid 1 per cent., or lead-water. The use of cold applications is often satisfactory as they usually at least relieve the pain. Others apply ichthyol ointment and recommend painting with tincture of iodine (a procedure to be avoided in the infant). The artificial hyperæmia of Bier seems to promise results.

C. OPHTHALMIA NEONATORUM

As in older children, blennorrhœa of the newborn is an acute infectious inflammation of the conjunctiva which is characterized by profuse purulent secretion and granular infiltration. The method of infection in the newborn, however, is unique and the disease must be classed amongst the infections due to parturition.

Symptoms.—In the great majority of cases the disease begins on the second or third day of life, with œdema and slight redness of the lids, usually of both eyes, however, in one fourth to one fifth of the cases only in one eye. The œdema gradually increases until the skin of the lids becomes extremely tense; the lids are no longer opened spontaneously and are separated with difficulty, by the physician.

At this time a fairly profuse, thin secretion commences, resembling in color washings from meat, and containing a few flocculi. Inspection of the conjunctiva shows severe hyperæmia and swelling, not confined to the palpebral portion and the fornix but extending also to the globe; here the process is usually least marked, but it occasionally leads to extensive swelling, limited sharply at the corneal margin (chemosis). Small hæmorrhages in the conjunctiva are not uncommon. Two or three days after the beginning of the disease the secretion becomes thicker, lemon- to greenish-yellow, creamy and very profuse. The œdema of the lids gradually diminishes, the redness subsides, and the surface of the conjunctiva, smooth up to this time, becomes granular; the fornix becomes thickened and plump and bulges forward on everting the lids. After two to four weeks the suppuration diminishes, the granulations on the conjunctiva subside and its surface becomes smooth again; the secretion, losing its strictly purulent character, becomes first muco-purulent and less profuse and finally catarrhal; the hyperæmia lessens and the conjunctiva returns to its normal state; scar formation does not usually occur, even after the severest processes.

In many cases the inflammation does not extend so far; the purulent secretion is scant and may even be entirely wanting; in other cases the manifestations are severer, the œdema especially extensive, the inflammation leading to the formation of pseudomembranes on the tarsal conjunctiva and occasionally to the occurrence of membranous tissue necrosis.

The severest complication is the involvement of the cornea in the inflammatory process: this has now, with the timely inauguration of the proper therapy, happily become a rarity. Infiltrations are formed at times on the margin and at times in the centre of the cornea; the superficial epithelium of the cornea becomes dull and suppurative solution of the tissues takes place with the formation of an ulcer which usually perforates. The central ulcers do not usually spread after perforation, but in some cases the entire cornea is involved. Marginal ulcers are easily overlooked when they are covered by the swollen conjunc-

tiva; they are either single or when multiple can become confluent, causing the loss of the entire cornea. The consequences of perforation differ according to its location; total or partial staphyloma, panophthalmitis with destruction of the bulb, capsular cataract, anterior synechiæ. The corneal involvement usually occurs between the 5th and 14th day of the disease. As a rule the earlier the cornea becomes involved the severer is the disease.

Ophthalmia neonatorum is often accompanied by disturbances of the nutrition of the child and by fever. Except for the extension to the cornea, *complications* are rare. One of the most important is arthritis, caused by the entrance of the gonococcus into the circulation. The *specific arthritis* has as its seat of predilection the knee-joint; it may, however, attack other joints, such as the wrist, hip, ankle and shoulder. Sometimes mono- and sometimes polyarticular, it leads to painful swelling in the neighborhood of the joints which become hot and œdematous. Active movements are either not carried out at all or else only within a limited range; passive movements are resisted and cause great pain. There is usually a serous effusion into the joint cavity. In some cases suppuration occurs in or around the joint. The arthritis runs a febrile course in some cases; in the majority, however it is afebrile. Permanent impairment to joint functions does not occur. Vignaudon reports muscular atrophies occurring as the result of this arthritis.

The causative agent of the ocular inflammation, the gonococcus, has been demonstrated in the joint fluid in a number of cases, first by Deutschmann; in two cases (Sobotka, Finger) streptococci were found with the gonococcus.

Gonococcus stomatitis is the rarest complication of ophthalmia neonatorum; it may occur from the infected tears running off through the lachrymal ducts, or possibly from contamination of the oral cavity directly. It is manifested by extensive exudation and purulent secretion; gonococci have been found in the secretion (Rosinski).

Etiology.—In the vast majority of cases conjunctival blennorrhœa of the newborn is produced by the gonococcus of Neisser. In 44 per cent. of observed cases Groenow demonstrated the gonococcus; Ammon in 56 per cent. and Haupt in 71 per cent. When we consider the fact that in cases of longer duration we are not able to find the gonococcus, the percentage of cases caused by the gonococcus must be even higher than the above. The remaining cases of purulent conjunctivitis in the newborn are caused by the bacteria of inflammation: pneumococcus, streptococcus, bacillus coli, bacillus pseudo-influenzæ and possibly staphylococcus pyogenes aureus and others. Saemisch advises cataloging the cases of purulent inflammations of the newborn not due to the gonococcus as acute blennorrhœic conjunctivitis, in contradistinction to acute gonoblennorrhœa.

Pathogenesis.—Infection of the conjunctiva of the newborn can take place in various ways. As a rule the infection takes place from a urethritis or vaginitis of the mother. Herewith the child may be already infected in utero or, through the agency of the examining physician or midwife whose fingers carry the infection from the vagina to the eyelids of the child, and possibly also through infected amniotic fluid. Usually, however, the child is infected during the passage of the head through the birth canal, when the lids become covered with the secretion which reaches the conjunctiva when the eyes are opened.

In many cases the child is infected post partum from the hands of the nurse or mother. In institutions children of healthy mothers are sometimes infected indirectly from other children infected with blennorrhœa.

Experience teaches that the cases of ophthalmia arising from infection during birth only rarely begin later than the fifth day.

Diagnosis.—The diagnosis of gonorrhœal ophthalmia is easily established. It can easily be differentiated from simple catarrh caused by irritation (nitrate of silver catarrh) of the conjunctiva and from purulent conjunctivitis caused by other than gonorrhœal infection, by means of bacteriological examinations. In some cases an acute dacryocystitis, such as occasionally occurs in the newborn as the result of a congenital closure of the lachrymal duct, may give rise to confusion with gonoblennorrhœa. With this condition, however, the disease is always unilateral and by pressure over the tear sac pus may be expressed.

Frequency.—Ophthalmia neonatorum is very prevalent, but owing to the prophylactic measures employed in maternities it has become less frequent. Notwithstanding this, however, according to the statistics of Cohn for the year 1906, there are still 31 per cent. of the inhabitants of asylums for the blind in Germany, who owe their loss of vision to gonoblennorrhœa.

The **prognosis** is good, when timely, suitable treatment is instituted. The non-gonorrhœal purulent inflammations lead to involvement of the cornea less often than the gonorrhœal.

Prophylaxis is most important. Excellent results have been attained from the procedure introduced by Credé. According to his advice, the infant should be cleansed and bathed immediately after birth; the lids cleansed externally with sterile water applied with cotton pledgets; then one drop of a 2 per cent. silver nitrate solution should be applied to each eye by means of a glass rod; this application should not be repeated.

Credé's method has given admirable results and has unquestionably reduced the frequency of blennorrhœa neonatorum. Since, however, its employment is not absolutely preventive, it is recommended to use repeated disinfecting vaginal douches during delivery. Many clinicians

lay especial value on the cleansing of the lids externally with disinfecting fluids immediately after birth, and some even prefer it to Credé's method. Objection to the latter method is often raised on the ground that it frequently leads to irritation of the mucosa (silver nitrate catarrh). On these grounds a 1 per cent. solution of silver nitrate is often used. Substitutes for the nitric acid salt of silver seem only to be less effective than the latter itself.

Credé's method has doubtless been of great value in maternity hospitals. The question as to whether it should be generally employed in private practice and possibly made obligatory, is still under lively discussion. It should be used, however, in conjunction with vaginal douches, in every case in which the physician or midwife detects a purulent vaginal discharge in the mother before delivery.

Late infections can be absolutely avoided by scrupulous cleanliness on the part of nurse and attendants. Nurses and mothers should be admonished to cleanse their hands thoroughly every time before handling the child. It is self-evident that mother and child should not employ in common such things as washing utensils, syringes, cotton, etc.

Therapy.—The treatment of gonoblennorrhœa should be directed toward lessening the inflammation and removing as quickly as possible the accumulating secretion. To prevent corneal complications ice compresses are used in the first stages of the disease and kept up until the secretion becomes slight and its purulent character has disappeared. For this purpose small gauze or lint compresses folded four to eight times are used. Many of these are prepared, put on ice and changed every three to five minutes. Since the gauze or lint absorbs the secretion, the compresses must be frequently replaced by new ones. When changing the compresses the secretion should be wiped away with sterile cotton. The secretion collecting in the fornix should be removed by douching. The douches should be used very often when suppuration has begun, every one-half to one hour, day and night. It is in this connection of great importance to avoid any, even the slightest, injury to the corneal epithelium, in order to avoid paving the way for infiltrations of the cornea.

The following solutions are recommended for douching: potassium permanganate in a red (3 per cent.), or in very dilute solution; sublimate 1:5000; boracic acid three per cent; oxycyanate of mercury 1:2000; also physiological saline solution; boiled water and others.

With the beginning of the secretion, the conjunctiva should be swabbed daily with a 2 per cent. solution of silver nitrate. Touching the cornea with the silver solution and the use of saline to neutralize it, should be carefully avoided. In case the inflammatory signs and the secretion should not soon diminish, one can employ a 3 per cent. solution of silver nitrate for application to the conjunctiva. If only one eye

is attacked the healthy eye can be protected against infection by dropping into it daily one drop of a 1 per cent. silver nitrate solution. Bandaging the healthy eye is very efficient, but irritations of the skin and also of the conjunctiva occur quite readily under the bandage. Notwithstanding this, bandaging the healthy eye is often advocated when only one eye is affected.

When the cornea is involved, 1 per cent. atropine solution (when the ulcer is marginal, 1 per cent. eserin) should be dropped into the eye. moreover the use of the ice compresses must be discontinued; but not the application of silver nitrate. One should consult the text books on ophthalmology for further information on this topic.

Arthritides are treated by application of liquor aluminii acetici (P. G.) diluted eight times. It is best first to anoint the skin, over the diseased joints, with vaseline.

Purulent effusions into the joints, manifested by extensive inflammatory signs and established by exploratory puncture, are to be incised under aseptic precautions. Salicylates may be tried but seem to accomplish very little.

D. SEPSIS IN INFANCY

The lack of unanimity concerning the septic diseases, renders it advisable at the outset to fix distinctly just what is understood by the term "sepsis."

From a great number of definitions which up to the present have not fully succeeded in classifying the subject, we prefer that of Lenhartz, and will, therefore, understand with him "under the caption sepsis, all general diseases caused by the pyogenic cocci and other equivalent bacteria." Whereas, rather inappropriately, the septic processes without abscess formation are to be termed sepsis, the ancillary term "with metastases" is to be employed when reference is made to what has heretofore been known as pyæmia (metastasizing sepsis). We, however, only speak of metastasizing sepsis when proof is present either during life or at necropsy that the abscess has not been formed by direct contiguity through the lymph- and tissue-spaces, but has occurred through the medium of the circulation. Kocher and Tavel speak of bacteriæmia when bacteria have gained entrance and circulate in the vascular system, and of toxæmia when only products of bacterial metabolism have been absorbed into the circulation. On account however of the varying symptoms of sepsis in the first months of life, often difficult of interpretation, we must limit the designation sepsis without exception to those disease pictures in which proof has been furnished of the presence of bacteria in the blood. When in a given case no proof is adduced or can be furnished of the presence of bacteria in the circulation, we are only justified in classifying it under the head of sepsis when

it agrees in symptom-complex, course, and possibly in anatomical findings, with those disease pictures in which general bacterial infection has been demonstrated.

The question to what extent we are justified in attributing the symptom-complex of sepsis to a mere toxæmia must be held in abeyance. It is to be expected that improvement in our bacteriological technique will enable us to reserve the designation sepsis for that symptom-complex with which the entrance of pyogenic organisms into the circulation has been demonstrated. This proof can already be furnished in most cases, if not during life at least at necropsy.

Cause of Sepsis.—Sepsis in the infant, as in the adult, may be caused by a variety of bacteria. First and foremost the so-called pyogenic cocci are to be named. The staphylococcus pyogenes albus and aureus, the streptococci (among which the intestinal streptococcus of Escherich occupies a prominent place), the diplococcus pneumoniæ (Fraenkel-Weichselbaum), bacillus coli communis, bacterium lactis aerogenes, bacillus enteritidis Gärtner and related strains, bacillus pyocyaneus, the proteus group, more rarely the gonococcus, the influenza bacillus of Pfeiffer and possibly the bacillus of Friedlander and the meningococcus of Weichselbaum.

Varieties of Sepsis.—Sepsis may be primary, or secondary to a pre-existing disease. It is usually caused by a single organism and only occasionally, although seemingly more often in the infant than the adult, there is a polymicrobic infection.

We must differentiate a hetero- and auto-infection just as in the adult. According to Kocher and Tavel we speak of hetero-infection when the cause of the disease comes from without and of auto-infection when it is already present in the organism under normal conditions, before the disease. The majority of infections are hetero-infections. The infant with its special susceptibility has ample opportunity for contamination with infectious agents; especially those from the air; also through its clothes and further through its food, which in infancy is usually milk. Mothers' milk is much better protected against infection than cow's milk. We know, however, that the milk of healthy as well as septic mothers contains bacteria. The bacteria enter the lacteal ducts from without; according to Basch and Weleminsky bacteria never invade the milk from the circulation unless there has been some disturbance of the structure of the breast (*e.g.*, hæmorrhage). Pyogenic bacteria are regularly found in the milk of animals. The infant is also exposed to infection from the water used in cleansing its mouth and perhaps even from the water of the bath; this latter source of infection has hardly been established and has been at all events much over-estimated in importance. The newborn, moreover, is exposed to infection from the lochia, which normally contains pathogenic bacteria; this infection

either takes place directly during the passage of the child through the birth canal, or indirectly, through carrying the lochia to the body of the child by mother or nurse or on instruments or bandages.

The newborn, moreover, as also the older child, is exposed to infection from other children, especially infants suffering from septic or inflammatory disease; the infection being carried by physicians, attendants and on utensils. The frequent occurrence of veritable epidemics of sepsis of the newborn in maternities can be easily understood.

Susceptibility.—Infants possess seemingly a relatively low resistance to septic infection; the younger the child the less the resistance and the less mature the child at birth the less its resistance. Thus the premature infant is especially menaced by septic infection. It is also a very striking fact that infants seem to become septic less often when at home than in institutions. This reminds us of the behavior of puerperal fever; yet, whereas, puerperal fever belongs to the rarities in well conducted maternities, sepsis neonatorum is still not an uncommon occurrence and epidemics of this disease are a menace to every hospital for the care of infants. The low protective power which the nursling develops against septic disease is partly attributed to the undeveloped condition of its organs. Thus the lymph-nodes, which play a prominent part in the defence against sepsis, are of little or no importance to the nursling and the absence of even regional lymph-node enlargement is the rule in sepsis neonatorum. Further, we must consider the undeveloped condition of the skin, which seems especially adapted for protection against infection (according to Hulot the stratum corneum is scantily developed in the newborn). The epithelium of the gastro-intestinal tract is also said to be, in contradistinction to the adult, pervious for bacteria even without any lesion. For certain animals it has been firmly established that the intestinal mucosa of the newborn is not impervious to the passage of certain bacteria; whereas this is not the case in the adult animal; to what extent this holds good in human beings has not been established. The middle ear is also not fully developed, the tympanic cavities being filled with an embryonal tissue resembling the jelly of Wharton in its structure. We can attribute the susceptibility of the young infant to septic infection principally, perhaps, to its insufficiently or scantily developed capacity for manufacturing protective substances (Halban, Landsteiner).

The well-established observation that artificially fed infants often succumb to septic infection, whereas breast-fed children are relatively seldom attacked (which holds good for the nursling after the end of the second month) must have direct relation to the food. Explanatory of this, we can refer to Moro's investigations concerning the transmission of alexins from the mother's milk, rich in these substances; as cow's milk is much poorer in alexins we could thus explain the increased protection of

breast-fed children. The belief is also advanced that the cells of the artificially nourished child are so taxed by assimilation of the foreign or aspecific ("artfremd") food that they can elaborate less protective substance against possible infection.

In the nursling, during the first days of life, the umbilical cord and the wound left after its separation are especially liable to infection. Infection of the newborn is further facilitated by the physiological desquamation of the skin and mucous membranes. After consideration of all these conditions it seems clear that the newborn, particularly the premature newborn is especially susceptible to general septic infection.

The susceptibility for sepsis is doubtless increased by the presence of other diseases, among which hereditary syphilis and intestinal affections are most important in infants.

Portals of Entry.—The newborn infant may be born septic. The virus can pass to the fœtal circulation through the placenta, when bacteria, which have broken through the placental vessels, circulate in the mother's blood. Such cases have been verified not only for the pyogenic cocci but also for other bacteria, *e.g.*, bacillus typhosus, diplococcus pneumoniæ, etc. The newborn can also become septic through aspiration of infected liquor amnii, as when the bag of waters ruptures too early. The newborn can further be infected during its passage through the birth canal.

Dubrisay reported a case of purulent vaginitis in the mother; sepsis of the child; death 11 hours after birth with pleurisy and pneumonia. Congenital and placental infections and sepsis acquired during the birth are frequent experiences.

After birth, the *umbilical cord* is the most frequent point of entry for sepsis. Infection, moreover, takes place usually before the separation of the cord. After separation of the cord the navel wound, for reasons given in the chapter on diseases of the navel, often furnishes the gateway for local and general infection. Next in frequency as an entrance port for infection comes the skin, its physiological peculiarities in the newborn, the many traumata to which it is exposed and which so often lead to superficial diseases (eczema, furunculosis) predisposing it to septic infection.

Fissures, slight tears, superficial abrasions of the epithelium, such as are caused by mechanical cleansing, decubitus on the heel or above the internal malleoli or over the sacrum, such as often develop in children suffering from disturbances of nutrition, are convenient gateways for the entrance of the virus. The mucosa of the oral cavity is very often the starting point of sepsis (Epstein). The physiological shedding of the mucosa in the newborn, mechanical abrasions due to cleansing of the mouth, fissures of the mucosa, the so-called Bednar's aphthæ, septic pseudodiphtheritic inflammation of the oral mucosa (Epstein),

thrush, and the various forms of stomatitis and gingivitis can all lead to sepsis. The pharyngeal and nasal mucous membranes, as a rule only when locally diseased, are also at times the starting point of general infection. It is worthy of note that the *tonsils* have only in the rarest instances been considered the entrance for general septic infection. In very rare instances sepsis arises from the conjunctiva and that too, only when it is the site of some inflammation, gonococcus or other.

The *ear*, which is a frequent site of local disease in the infant, can also be the source of a sepsis prone to have the clinical picture of purulent meningitis (Scherer).

The mucosa of the *gastro-intestinal tract* has been regarded by many as the starting point of septic processes. Sevestre and others have considered the inflamed intestine to be the point of entry and Czerny and Moser have held gastro-enteritis to be the primary focus of a general sepsis. Proof however, has not yet been adduced and only the few well established cases in which the intestinal streptococci of Escherich have lead to sepsis serve as a foundation for the opinion that the newborn and young child can be infected with sepsis starting from the injured intestinal mucosa.

Very much more importance must be attributed to the *lungs* than to the gastro-intestinal tract, as furnishing the primary focus of sepsis (Fischl).

It is usually either a bronchitis with necrosis of the epithelium or else more or less extensive inflammatory foci, from which the infection spreads by way of the lymphatics (Fischl).

In some cases the infection can be referred to *injury at birth;* namely, when the injury has led to local inflammation. In other cases the skin is the gateway for the entrance of the infection; and diseases of the skin often furnish the chance for septic infection.

In relatively infrequent instances local infections of the vulva, more frequently diseases of the bladder, and cystitis, by extension to the upper urinary tract, can give rise to septic infection (Escherich, Trumpp). It is worthy of note that this mode of infection (cystitis) is almost without exception confined to female infants.

In many cases the starting point of the sepsis remains unknown: we may, therefore, speak of a cryptogenic sepsis.

Clinical Picture.—Sepsis occurs in various forms in the infant, dependent on the origin of the infection, the age of the child and the virulence of the bacteria.

We must first note that there are many cases which run their course practically *without symptoms*. With or without a demonstrable primary disease, while apparently well, the child goes into sudden collapse and dies, the temperature falling rapidly. In such cases the diagnosis of a general infection can only be suspected, though somewhat more strongly

when the newborn is premature. In other cases, however, the course of the disease is stormy, with a high fever, vomiting and severe diarrhœa, so that the sepsis runs its course under the clinical picture of an *acute gastro-enteritis* (v. Ritter, Epstein). In a third group of infants, we have fever, ashen gray pallor of the skin, hæmorrhages in the skin and organs, severe inflammatory signs at the navel, on the skin, in the lungs, gastro-intestinal or urinary tract. Added to these there are severe disturbances of the central nervous system which can also quite dominate the picture, so that the disease can simulate severe intoxication or *meningeal disease*. In other cases purulent metastases form the salient features of the disease or else—and especially in asylums—pulmonary symptoms are so prominent that the disease runs a course under the clinical picture of a *pneumonia*. Of special importance are the cases in which hæmorrhages into the skin or internal organs form the most salient and often the only symptom of septic disease. A number of cases which run their course under the picture of melæna must be classed with sepsis. Other cases are classified under the heading of "umbilical hæmorrhages" because the bleeding from the navel is the dominating and perhaps the only symptom and because no proof of sepsis is sought for or furnished either during life or at necropsy.

The probability of sepsis increases when the hæmorrhage is not single or from only one organ, but multiple. This leads us to the symptom-complex which has taken a place in the literature under the title of Buhl's disease or acute fatty degeneration of the newborn. The cases coming under this title occurred in children born at term, asphyctic for some unknown reason, and often dying without any attempt at respiration. The children which were resuscitated breathed badly, remained cyanotic, hæmorrhages appeared in the skin and mucous membranes, bloody vomit, bloody fluid evacuations and umbilical hæmorrhages occurred and the infants rapidly died. In case they lived on for a few days longer, severe anæmia, icterus and sometimes also anasarca occurred and then death in collapse.

At necropsy, beside countless hæmorrhages in the organs, there was found fatty degeneration of the cells of the pulmonary alveoli, of the muscles, the heart, liver and the epithelium of the uriniferous tubules.

The disease is said to occur sporadically and to closely resemble the disease of animals known as "spring-halt," in its manifestations and pathological anatomy. However, Bollinger proved that this latter disease as it occurs in foals is rarely an umbilical sepsis. It is highly probable that the symptom-complex described by Buhl is nothing else than sepsis, which it so closely resembles.

The clinical picture which Winckel described as icteric cyanosis or cyanosis icterica perniciosa cum hæmoglobinuria (also known as epidemic hæmoglobinuria), resembles sepsis in many aspects. Winckel

first observed this disease occurring as an epidemic in the maternity at Dresden, and since then only a few cases, also sporadic, have been reported.

These cases occurred in vigorous full-term children during the first days of life, in whom the principal manifestation was a yellow, icteric, and then deep blue discoloration of the entire cutaneous surface and of all the mucous membranes, just as with the severest cyanosis; and further a brownish color of the urine. The urine contained hæmoglobin, blood corpuscle casts, renal epithelium, bacteria, urate of ammonia, and small quantities of albumin. The children had little or no fever, rapid respiration and died, sometimes in convulsions. The blood was markedly thickened, contained numerous granules and a slight increase in the number of leucocytes.

At necropsy besides the icterus, countless hæmorrhages were found, especially in the mucous and serous membranes; also fatty degeneration of the organs and, especially characteristic, masses of granular hæmoglobin in the kidneys and spleen. In all cases, with one exception, the umbilical vessels were found to be healthy.

In a similar epidemic reported by Kamen, in which, however, hæmoglobinuria was absent, a bacillus was found in the organs and blood, which Kamen considered identical with the bacillus coli communis. Kamen found the same bacillus in well-water; according to his opinion the children were infected through cleansing the mouth. After the well had been closed up the epidemic ceased. As Epstein has already assumed, Winckel's disease is also nothing more or less than sepsis.

The classifying of these cases under a separate head is hardly justified, as no proof has been furnished of the presence of a hæmoglobinuria and moreover the presence of red blood corpuscle casts argues against a hæmoglobinuria; the finding of brown granules in the urine and kidneys is of no import since no chemical examination was made to determine whether or not they were composed of blood-pigment.

Symptoms.—1. *Fever.* This is not a constant manifestation. A rise in temperature, at times very high, occurs at the onset in the majority of cases. The further course is then either afebrile or else attended by a very irregular fever. Chills never occur. Toward the end of the disease a markedly subnormal temperature is the rule.

2. *Sensation* is benumbed in many cases; the children are at times comatose and at times show great unrest, jactitation, tremors and prolonged, severe, unvarying cries which are the expression of a state of excitation; this state sometimes alternates with profound apathy in which the reflexes are diminished and may be totally absent. Convulsions are rare. Upward rotation of the bulbi with open eyes, as in sleep and flaccidity of the muscles occur; but more often pseudotetanic, spastic conditions of the muscles of the extremities, trunk, neck and

head; with trismus, rigidity of the neck and extreme flexion of the hand and finger-joints, which is more frequent the younger the child. Paralyses do not belong to the usual picture of sepsis and depend on complications with meningitis or encephalitis.

3. The *skin* presents varying signs. Children in the first weeks of life usually show a marked icterus, which may, especially with umbilical sepsis, attain the degree of a bronzing (Porak and Durante). Older infants have often a livid, ashen-gray color which easily becomes bluish (cyanosis) on the distal parts of the body and on the mucous membranes. There is often œdema of the feet, over the tibiæ and in the pubic region. In some instances sclerœdema and more rarely sclerema occur toward the end of the disease, especially in premature children, during the first months. The hæmorrhages are characteristic and very important diagnostically; they spread over the trunk and extremities, sometimes as small petechiæ and sometimes as more or less extensive effusions. Furuncles and extensive skin abscesses—as a rule not embolic but occurring through infection from without—are frequent findings and also often form the entrance point for the infection. Bed sores occur not uncommonly over the parietal bones, the sacrum, the heel, the internal malleoli and more rarely the elbow; the sores soften and lead to deep ulcerations which sometimes extend to the periosteum and cause necrosis of the bones. Erysipelas is not rarely added to the above, especially in cases of umbilical sepsis. The various septic erythemata are characteristic; they occur at times as small rose spots, at times as a diffuse redness, seldom similar to erythema multiforme and only exceptionally as an urticaria; their tendency is to spread over the trunk and extremities. At times blebs, with purulent or serous, rarely bloody, contents, are formed.

4. The *mucous membrane of the mouth* is very often loosened, especially in young infants, and not rarely covered with hæmorrhages. Fissures in the corners of the mouth, catarrhal inflammations with or without thrush, processes leading to necrosis of the mucosa, which are sometimes followed by necrosis of the jaw-bones; inflammations and suppurations of the salivary glands (especially the parotid) which on pressure fill the mouth with pus; all these are among the most frequent occurrences. Catarrhal rhinitis sometimes causes profuse purulent discharge with the formation of fissures on the alæ nasi and more rarely severe epistaxis. In some cases the fissures or the inflamed or necrotic mucous membranes bleed, thus at times leading to the diagnosis of melæna.

5. The *eyes* are not usually involved in the systemic infection. Retinal hæmorrhages have been found repeatedly in the newborn and are of value diagnostically. Hæmorrhages from the lids, at times uncontrollable, are, according to Ritter, of septic origin in the majority of

instances in which there is no primary local disease (blennorrhœa, etc.). Otitis media occurs very often; but extension of the process to the bones, sinuses, brain or meninges belongs to the rarest complications.

6. The *respiratory organs* are most severely involved in the symptom-complex of sepsis. Even in uncomplicated cases dyspnœa with very rapid breathing is present as an index of a severe intoxication. Bronchitis and pneumonia, which are only demonstrable when somewhat extensive; multiple abscesses of the lungs, clinically not demonstrable; serofibrinous and purulent pleurisies, all belong to the most frequent occurrences. When they form the only salient clinical feature the disease is termed "septic infection with pulmonary symptoms" (Fischl).

7. *Pericarditis* occurs quite often, as an involvement of the *circulatory apparatus*, in consequence of the general infection. It usually arises by extension from the pleura, or more rarely from the mediastinum. Endocarditis has been observed several times, on the whole, however, rarely. In the diagnosis of this complication in infants we often encounter insurmountable difficulties (Finkelstein). The behavior of the pulse is in no way characteristic. Just as in all severe diseases of the infant, cardiac weakness easily comes on and either leads acutely to death or else persists for days, accompanied by a subnormal body temperature.

8. The *gastro-intestinal* canal is very often involved in the clinical picture of sepsis. Vomiting and diarrhœa are at times the only, often the most striking symptoms. The sepsis not uncommonly runs its course from the very beginning under the clinical picture of a gastro-intestinal catarrh; more frequently, however, severe diarrhœas occur during the course of sepsis, and, what is worthy of note, in artificially fed as well as breast-fed infants (Ritter *et al.*).

The vomitus is bile stained in some instances, in others it is colored from blood-red to brownish, the stools are fluid or soft, yellow or green and often there is an admixture of blood, brown or blackish brown in color, rarely dark red (melæna). The abdomen is distended very frequently and the peristalic action very lively; at times intestinal paralysis with tremendous distention of the abdomen occurs, pushing up the diaphragm and causing dyspnœa; purulent peritonitis occurs very often, especially in cases of umbilical sepsis. Recognition of the peritonitis, however, is difficult; fluid exudate is usually not present in demonstrable quantities. The presence of considerable tenderness over the abdomen may be considered as evidence of peritonitis.

9. The *spleen* is frequently enlarged, but the swelling is of no value diagnostically, as it occurs in the nursling in so many other conditions.

10. The *liver* seldom shows any clinical signs except the icterus, the import of which has already been discussed. The edge of the liver is

palpable in the healthy nursling when the abdomen is free from distention; therefore, the fact that the liver is palpable should be used cautiously for diagnostic purposes.

11. The *urine* usually contains albumin, rarely sugar (milk-sugar). The albuminuria is either an expression of a toxic degeneration of the kidneys or of a true, rarely hæmorrhagic, nephritis or a pyelocystitis. In children of the first weeks of life who have had icterus, bile-pigment is often found in the urine (see chapter on icterus neonatorum). In many cases hæmoglobin in solution and in pigment granules has been found (Winckel's disease). The urinary sediment should be examined in every case and gives findings corresponding to the involvement: hyaline, epithelial or granular casts, casts of blood corpuscles, pus cells, either isolated or in clumps, epithelial cells and leucocytes.

The sexual organs as a rule are normal, although Ritter reports genital hæmorrhages and vaginal catarrh occurring during the course of septic infection in the newborn.

12. The *bones and joints* show severe changes in occasional cases; periostitis and osteomyelitis occur rarely in the infant; multiple inflammatory foci in the joints, especially the hip and shoulder joints (Czerny and Moser) betray their existence by the immobility and the œdema of the affected extremity and more rarely by a reddening over the joint. Pressure over the diseased area and passive movement of the affected extremity elicit expressions of pain. With appropriate passive motion at the ends of the bones one is often able to elicit a fine crepitation, a sign of epiphyseal separation, which does not occur with hereditary syphilis alone.

13. The *blood* may show startling changes. A decrease in the number of erythrocytes is frequent; a polynuclear leucocytosis has been found more rarely. Noteworthy is the deficient coagulability of the blood, which must be attributed to the action of toxins and reminds one of the behavior of the blood when peptone and certain other poisons (leech extract, etc.) have been injected. In some cases (Winckel's disease) the blood was "syrup thick," and microscopically countless blood granules, due to destruction of the red cells, were found. In other cases hæmoglobin and also methæmoglobin were demonstrated in the serum with the spectroscope.

Anatomical Findings.—The pathological changes found in sepsis of the newborn, with the exception of certain characteristics due to the peculiar behavior of certain organs in infancy, are the same as those in sepsis of the adult. In the acute cases and those without metastatic abscesses there are two principal lesions regularly found; namely, hæmorrhages and parenchymatous degeneration of the heart muscle, liver and kidneys. The hæmorrhages are scattered throughout practically all the organs; aside from the clinically demonstrable hæmor-

rhages in the skin, mucous membranes and retina, they are found regularly in the dura, sometimes in the pia and more rarely in the brain substance.

The findings in the various organs agree and vary with the clinical symptoms and there will be mentioned only those results of pathological examination to which no reference has been made in discussing the clinical manifestations.

The brain is often œdematous and hyperæmic; the meninges are congested and scattered with hæmorrhages. Hæmorrhages in the brain substance itself are not so common; encephalitis and meningitis have been observed at times, brain abscesses rarely. Foci of lobular pneumonia are very often demonstrable, as also atelectatic areas, small multiple embolic abscesses and frequently also infarctions. Fatty degeneration of the alveolar epithelium is not uncommon in the form of sepsis described as Buhl's disease. The pleuræ are often the seat of inflammation, usually serofibrinous or purulent. The heart muscle, in consequence of the intoxication, shows parenchymatous or fatty degeneration; it is pale and often shows the so-called tiger markings; the valves are only rarely the seat of an inflammatory process, the pericardium much more frequently. The liver usually shows parenchymatous degeneration. Not uncommonly, as the result of an umbilical phlebitis, we have multiple abscesses in the liver, which in life give rise to no symptoms. The spleen shows signs of acute or chronic swelling. The gastro-intestinal tract may be found either normal or slightly inflamed. In occasional cases we have a pronounced acute gastro-enteritis and in these cases the mesenteric lymph-glands are found considerably swollen. Hæmorrhages are found very commonly in the mucosa as well as in the serosa of the stomach and the entire intestinal canal. The peritoneum is the seat of an acute inflammation practically only in cases of umbilical sepsis, otherwise it is normal. The kidneys show pathological changes in every case; at times only a parenchymatous degeneration and at times fatty degeneration with necrosis of the renal epithelium; hæmorrhages, round-cell infiltrations, interstitial inflammatory changes and diseases of the pelvis are the findings corresponding to the varying involvement of the urinary apparatus in the septic process. Even in the milder cases we very often find hæmorrhages in the bone marrow and sometimes metastatic periostitis, osteomyelitis and arthritis; the latter with either serous or purulent effusion. At the umbilicus not uncommonly we find the changes described in the chapter on diseases of the umbilicus.

The **diagnosis** of sepsis must in general be considered as difficult. Bacteriological examination of the blood furnishes the most reliable results. Inasmuch, however, as it is always necessary to draw off considerable quantities of blood and as this can only be done unimpeachably

by puncture or incision of a vein and not from the ball of a finger or toe, it is evident that this examination can only be carried out in a small percentage of infants during life. Added to this is the fact that bacteria are not found in the blood in life in a considerable percentage of cases of sepsis. It is recommended to make the blood examination during the death agony or immediately post mortem, a method of procedure which can usually be carried out with infants. Sometimes the bacteria may be found in numbers in cover-slip preparations from the blood of the cadaver. In some cases information may be furnished by puncture of organs which are the seat of metastatic inflammations and the bacteriological examination of the body fluids, only rarely the bacteriological examination of the urine which is drawn by catheter.

In the majority of cases, however, we must get along without bacteriological examinations of the blood (lumbar puncture furnishes no certain evidence, since bacteria are found in the cerebrospinal fluid in the absence of sepsis, under certain conditions). Then the diagnosis must be made from the clinical information. When the primary focus is demonstrable, when the infants have fever, and metastases or hæmorrhages show themselves, we are probably justified in making the diagnosis. The examination of the retina, recommended by Herrenheiser and Fischl, may be of value diagnostically. However, we must not lose sight of the fact that in the newborn retinal hæmorrhages may also be caused by birth trauma. In some cases it is impossible in the absence of bacteriological anatomical evidence to decide whether or not we are dealing with sepsis. In acute cases sepsis must be differentiated from acute gastro-enteritis and pneumonia, and in children only a few days old, from atelectasis and cerebral or meningeal hæmorrhage; the cases running a subacute or chronic course must often be differentiated from chronic nutritional disturbances carrying secondary diseases in their train.

The **prognosis** is very serious; the more acute the course of the disease, the younger and more immature the affected infant and the more organs evidently involved, the more unfavorable the outlook.

Prophylaxis and Treatment.—Since sepsis occurs especially where children are cared for in numbers, as in institutions, it behooves us to employ all those means which have been so effective in the prevention of puerperal fever. The strictest asepsis in the care of the newborn is enjoined. The care of the child from the moment of birth should not be assigned to the same attendant caring for the puerperal woman. The umbilical dressing must be aseptic, the oral cavity should not be cleansed; the clothing of the infant should be sterilized and the hands of the attendant clean and disinfected when changing the clothes. All utensils should be individual for each child and should be kept sterile (bath-tub, basins, cotton, thermometer, etc.). In hospitals the isolation of all

nurslings is of special value (the box system of Grancher, or, still better, isolation cells or rooms). For the breast-feeding of infants, the breast should be carefully cleansed before each nursing and in artificial feeding the strictest asepsis of food, bottles and nipple must be carried out. Heubner has recommended that in institutions the feeding of children should not be entrusted to the attendants in charge of the cleansing of the children.

In the care of premature children, kept in incubators, it becomes unqualifiedly necessary to strive for strict disinfection of the incubator and a sufficient supply of clean air.

The **treatment** of the developed disease is purely symptomatic. Together with the combating of the individual symptoms one must devote attention to the care of the skin and the nourishment; artificially fed children should be furnished with human milk since through this the chances of recovery are increased. All abscesses must be opened and treated according to surgical principles. Bandages should be limited as much as possible in order that healthy areas of the skin may not be involved through the bandage. The heart's action should be carefully supported; one may employ strong tea, small doses of digitalis (0.05 Gm. ($\frac{3}{4}$ gr.) pro die in infusion) or digalen $\frac{1}{2}$ c.c. (♏ $7\frac{1}{2}$) internally daily, caffein (caffein sodium salicylate 0.05 to 0.1 Gm. ($\frac{3}{4}$ gr.–$1\frac{1}{2}$ gr.) pro die) or camphorated oil 0.3 to 0.5 c.c. (♏ 4–8) subcutaneously (possibly two to three times daily). The subcutaneous injection of physiological saline solution (nine-tenths of 1 per cent.) in amounts 20–50 Gm. (5–12 drams), according to age, is recommended by many. Just as with adults, colloidal silver may be tried and especially per rectum or by intravenous injection of 0.1 Gm. ($1\frac{1}{2}$ gr.) (Finkelstein). The use of specific immune sera has up to the present time shown no beneficial results.

V. MELÆNA NEONATORUM

The name melæna neonatorum is not applied to any one disease as an entity. It rather serves to cover a symptom-complex, the loss of blood from the gastro-intestinal tract, either from the stomach by vomiting, or from the rectum, or both. One is justified in expunging melæna from the category of diseases of the newborn. However, inasmuch as loss of blood from the gastro-intestinal canal often forms the most marked and at times the only demonstrable symptom in certain maladies of the newborn, we give this symptom-complex special consideration. We will endeavor, therefore, to give a brief description of this symptom-complex and its consequences and, by comparing its clinical picture with the hitherto known anatomical findings, to show the method by which the examining physician can make a diagnosis of the underlying disease. We must again emphasize the statement that a diagnosis of melæna is unjustifiable and that endeavor must be made in

every instance to discover the disease responsible for the hæmatemesis or the hæmorrhage in the intestinal canal. There are three varieties of melæna,—spurious, symptomatic and true. Spurious melæna designates the loss of blood from the gastro-intestinal tract when the hæmorrhage does not really originate in the mucosa of the gastro-intestinal tract. Thus we know that epistaxis frequently causes the vomiting of blood in the newborn. The epistaxis, moreover, is often overlooked, because the blood instead of escaping from the anterior nares runs backward into the pharynx and œsophagus and thence into the stomach. In such cases one is occasionally able to see streaks of fresh blood on the posterior pharyngeal wall (Swoboda). This epistaxis in children, however, depends upon various pathological processes in the nasal mucosa, syphilitic rhinitis, ulcerations with septic processes, nasal diphtheria (observed in syphilitic children, Swoboda). In still other cases the blood comes from the mucosa of the lips or mouth. Ulcers whose seat of predilection is the angle of the mouth, Bednar's aphthæ and stomatides, especially such as tend to necrosis, must be taken into consideration. In other cases spurious melæna is due to wounds of the buccal mucosa; such wounds may be caused during delivery by the finger of the accoucheur; or later, in the bloody separation of an adherent frænum of the tongue, an operation which was formerly extensively performed.

It could only be under the most complicated conditions that a pulmonary hæmorrhage in the newborn would lead to the vomiting of blood. However, pulmonary hæmorrhages have been observed in the newborn (Billard, Barthez and Rilliez, and recently by Esser), but to my knowledge hæmatemesis is not mentioned in the report of these cases, all of which ran an extremely rapid course without cough. However in older children the passage of blood from the stomach or intestines may occasionally be observed with pulmonary hæmorrhage.

Not infrequently the hæmorrhage does not originate in the child at all but in the mother. Fissures of the maternal nipple bleed during the act of nursing and the newborn swallows maternal blood, which at times is vomited or colors the feces black. In such cases however, there can be but a scanty admixture of blood. In some cases *spurious melæna* is attributed to the swallowing of blood during birth, for example, with premature detachment of the placenta. In case spurious melæna can be excluded, one then has to deal with a hæmorrhage originating in the blood vessels of the gastro-intestinal tract. We speak of *symptomatic melæna* when the gastro-intestinal hæmorrhage forms only one symptom of a demonstrable general disease; of *true melæna* when the hæmorrhage and its consequences dominate the entire disease picture. It is self-evident that a strict alignment into one of the above classes is often impossible.

We shall discuss, first, the cause of such a hæmorrhage and then the diseases and conditions that can be considered responsible for its etiology.

Course.—Hæmorrhage from the gastro-intestinal tract usually comes on within the first four days of life, most often on the first and second day, rarely later. In Silbermann's collected report of 42 cases, the hæmorrhage commenced on the first day in eleven cases and on the second day in sixteen cases. Evidence of the bleeding is most often seen in the stools; sometimes the meconium is streaked with blood or covered with clots, or we find a blood-red halo around the stool on the diaper. The bloody evacuation is usually trifling at first, but often increases in amount so that the stool is made up entirely of large clots or else is liquid, dark red or almost black in color and contains small solid particles. In some cases (according to Silbermann, 23 per cent.) the intestinal bleeding is accompanied by hæmatemesis, in the minority (16 per cent.) hæmatemesis forms the only symptom. In these latter cases the child vomits a dark red or brown fluid in which there are many small clots. In case the child has already ingested milk, black or brown lumps are vomited, together with the discolored milk, shortly after the feeding. Sometimes, however, there are only small streaks of blood demonstrable in the vomitus.

Hæmatemesis and bloody stools may cease after a single occurrence; then, if no underlying disease be present, the child will show no signs of disease. In other cases, however, the bloody vomit and stools recur and then the inevitable consequences of severe loss of blood become evident; the temperature falls, the distal parts of the body become cooled off, the face takes on a waxen pallor, the pulse becomes hardly perceptible, the heart sounds weak and the respiration superficial; there is suppression of urine and refusal to take nourishment. Rarely there are convulsions. In case the bleeding stops, the infant may recover even in severe cases, otherwise it succumbs as a result of the loss of blood, or, recovering from this, dies from the underlying disease.

It is self-evident that the symptoms are appreciably different when we are dealing with a constitutional disease which has given rise to symptomatic melæna. Sometimes the bleeding lasts for only a few hours and sometimes for several days.

Causes of Gastro-Intestinal Hæmorrhage.—Formerly, melæna, like other hæmorrhages in the newborn, was attributed to a "hæmophilia." This view, however, is either not tenable at all, or else it holds good for only the rarest of cases. In the first place hæmophilia usually does not occur during the first months of life; secondly, in children that have recovered from melæna, the "hæmophilia" also disappears; further, hæmophilia is a disease which generally affects males; and, lastly, it is an hereditary disease transmitted through the mother. All these are reasons which, with a careful history, permit as a rule of the exclusion of

hæmophilia. It was thought necessary to assume hæmophilia when several cases occured in the same family (not hereditary). As a matter of fact it is rather striking that there are families in which several children have had melæna and died of it during the first days of life. J. Fischer reviewed the cases already reported and added his own observations occurring in the first two children of a family; he considered hæmophilia as the etiological factor in these cases. Proof of heredity, however, was not adduced; a third child in the same family had no melæna, likewise no hæmophilia. We must, therefore consider the assumption of a hæmophilia in these cases as entirely unwarranted and admit rather that the cause of melæna in such cases is not clear; since no autopsy report is given and no bacteriological examination was made, no well-supported opinion concerning the origin of the melæna can be given.

In other cases the hæmorrhage from the rectum or the hæmatemesis forms only a part of the symptom-complex of sepsis. Septicæmia often leads to hæmorrhages; this has already been shown in the chapter on sepsis. Multiple hæmorrhages belong typically to the clinical picture of sepsis of the infant; however, sepsis not infrequently occurs under the guise of a hæmorrhage from a single organ and then sometimes under the clinical manifestations of melæna. Klebs, Ritter and Epstein have shown the rôle that sepsis plays in the causation of hæmorrhages in the infant and the investigations of the last years have confirmed the opinion that the so-called "hæmorrhagic diathesis of the newborn," which leads to bleeding in various organs, is, in the vast majority if not in all cases, nothing other than septicæmia. The investigations of Gärtner, Neumann, Babes, Finkelstein and others have established this. More recently endeavor has been made to attribute melæna neonatorum to infection with certain specific organisms. Gärtner described a "melæna bacillus" which he found in two cases of melæna. Despite the lapse of ten years since his communication, no confirmation of his findings is at hand. It is certainly not to be doubted that certain species of bacteria are particularly prone to produce hæmorrhages with the infections which they cause; but the specificity of neither the "melæna bacillus" nor the so-called "bacillus of hæmorrhagic infection in the human" (Babes) has as yet been established. Moreover, we know that infection with the most diverse kinds of bacteria can lead to multiple or single hæmorrhages.

Next to sepsis we must consider hereditary syphilis as an important cause of gastro-intestinal hæmorrhage. According to earlier reports (Behrend and others) and especially according to the thorough investigations of Mraczek, hereditary syphilis brings about changes in the walls of the small and medium sized vessels and of the capillaries, which lead to thickening of the intima, small-celled infiltration with subsequent connective-tissue formation, to thickening of the vascular wall and to a narrowing and even occlusion of its lumen. Thus venous stasis

and hæmorrhages ensue. These hæmorrhages occur also in the intestinal canal and Mraczek has reported such cases (Esser also recently reported one case). The assumption that these were cases of sepsis, which develops especially easily in syphilitic children, is negatived by the fact that, in some of Mraczek's cases, Kolisko and Paltauf were able to exclude sepsis by means of bacteriological examinations. In the vascular affections of hereditary syphilis, hæmorrhages can easily occur because of stasis and disturbances of the circulation, and at times syphilis runs its course under the clinical picture of melæna.

The gastro-intestinal hæmorrhages which Kundrat described occurring with syphilis of the liver are not to be attributed to a syphilitic affection of the vessels but rather to abnormal stasis in the portal circulation. However, not only the constitutional diseases just spoken of but also local diseases of the organs may lead to secondary (symptomatic) melæna. To this category belong first and foremost, congenital anomalies of the heart and large vessels; then diseases of the liver, *e.g.*, syphilis of the liver, which Kundrat advanced as the cause of melæna; further, tumors of the abdomen (cysts in Schukowski's case), then local diseases of the intestines and stomach, which lead to secondary gastric hæmorrhage. Cases of melæna are observed, however, with comparative frequency, in otherwise perfectly healthy children (true melæna). In these cases the hæmorrhage starts within the first four days of life, usually on the first or second day. In the cases terminating fatally, no constant findings in the gastro-intestinal tract have been shown at necropsy. In a part of the cases nothing which could have explained the hæmorrhage was found; in others, hyperæmia and stasis in the gastro-intestinal mucosa; and in still others, multiple hæmorrhages or hæmorrhagic erosions were found in the mucosa. In a few cases a small ulcer similar to the round ulcer of the adult, was found in the stomach or the small intestine (duodenum) or very rarely in the œsophagus. Multiple ulcers were rarely present.

Melæna is most easily explained in the cases in which there is an ulcer present. The erosion of a blood vessel in consequence of the tissue-necrosis, leads to bleeding which is often uncontrollable. For these cases, however, the question as to the origin of the ulcers must be raised; Landau advanced the hypothesis that emboli gave rise to them. The emboli are supposed to originate in a thrombosis of the umbilical vein or of the ductus arteriosus Botalli; the thrombus being swept into a branch of the pancreatico-duodenal or the gastric artery, occludes the vessel, thus causing necrosis and ulceration. The gastro-intestinal bleeding then ensues secondarily when the vessel is involved in the tissue-necrosis.

Kundrat brought forward against this theory, the fact that Landau had not demonstrated the embolic origin of the ulcers; that in one of

his own cases no embolism existed and that the sweeping of an embolus into the vessels of the intestine or stomach was highly improbable because the position, calibre and course of these vessels are very unfavorable for the lodgment of emboli. It is much more probable that the gastro-duodenal ulcers are not embolic in nature; they probably develop through hæmorrhages into the mucosa by reason of the softening and digestive action of the gastric juice on these infarcted areas (Kundrat). These ulcers are usually situated in the duodenum, less often in the stomach and rarely above the cardia in the œsophagus. Kundrat's conception is in part supported by a case of Chrzanowski's, in which there was bloody effusion throughout the entire thickness of the œsophagus above the cardia and only superficial defects were demonstrable in the epithelium. Further, the many cases of melæna, in which superficial hæmorrhagic erosions develop on a mucosa riddled with hæmorrhages, serve to substantiate Kundrat's position; in these cases the necrotic process has not progressed deeply enough to cause ulcer. That there are many cases in which hæmorrhages alone are found in the mucosa argues to this effect. In short, from hæmorrhage to erosion and then to ulceration we have only a series of pathological changes, the cause of which must lie in a hyperæmia of the gastro-intestinal mucosa. Moreover, in the cases in which no change has been found in the gastro-intestinal tract, we must, with Kundrat, hold that such a hyperæmia did exist during life which, however, at necropsy has disappeared. The cause of this hyperæmia is not clearly established; in explanation many theories have been adduced. A hæmorrhage in the gastro-intestinal tract can take place only under two conditions: (1) with a normal state of circulation and blood pressure, the vessel wall being diseased and thus offering inadequate resistance to the pressure of the blood; (2) with normal vessel walls, the blood pressure either local or general, being abnormally high. Of course in every such instance hæmatemesis does not necessarily follow, but on the contrary there is usually only stasis and slight hæmorrhage in the substance of the mucosa. Naturally, these two factors may coexist in any one case.

With constitutional diseases like syphilis, sepsis and hæmophilia, we assume that damage to the vessel walls is the primary and causal factor. In children otherwise healthy, however, it is unwarranted to assume a pathological change in the vessel walls. In such cases we must, therefore, predicate an abnormal stasis in the vascular system of the gastro-intestinal tract, which leads to hyperæmia and hæmorrhages in the mucosa or directly to the outpouring of blood on its surface.

The hyperæmia and stasis can in turn be caused: (1) by compression of the cord during labor; (2) by post partum asphyxia; (3) by insufficient respiration, such as occurs with pulmonary atelectasis, (4) by congenital anomalies of the heart and vessels; (5) by cerebral

and meningeal hæmorrhages; (6) by local circulatory disturbances in the abdomen (*e.g.*, with cirrhosis of the liver). It is well established that hæmorrhages do occur in the various organs of asphyctic children, of children that, in consequence of some obstruction to respiration, breathe only very superficially. But it has not yet been demonstrated that cerebral hæmorrhage in the newborn can actually give rise to melæna. The interesting experiments instituted by Brown-Sequard, Schiff and Epstein and elaborated by Klosterhalfen, were carried out on young animals by v. Preuschen and Pomorski; they showed that injuries of, and hæmorrhages into, various parts of the brain lead to hæmorrhages in the gastro-intestinal canal. This probably depends upon a disturbance or a paralysis of the vasomotor centre, which in turn leads to atony of the vessels, stasis and hæmorrhages. Therefore, since v. Preuschen found cerebral hæmorrhage in two cases of melæna, he considers himself justified in attributing melæna, in a part of the cases, to cerebral hæmorrhage. It is, however, possible that the cerebral and intestinal hæmorrhages exist coördinately, both being produced by the same cause; this question has not yet been clearly settled.

The Diagnostic Import of Gastro-Intestinal Hæmorrhage.—In every case of melæna an effort must be made to establish its cause. Spurious melæna is rather easily excluded; to this end careful inspection of the nose, buccal cavity and the posterior pharyngeal wall must be made in order to exclude these as the source of the blood. Examination of the maternal breast gives evidence as to fissures of the nipples. In case spurious melæna can be excluded, we must assume that the seat of the bleeding is in the gastro-intestinal tract. Then attention must be given to the signs by which hereditary syphilis can manifest itself in the newborn (see chapter on hereditary syphilis). Should there be neither clinical nor anamnestic evidence of the presence of syphilis, we must by means of the history, endeavor to exclude or establish a family and hereditary hæmophilia. However, in every case, even though evidence for the existence of syphilis or hæmophilia be at hand, we must endeavor to settle the question, whether sepsis may or may not be the principal causal factor. Consideration of the symptoms of sepsis, as detailed in the preceding chapter, will decide for us in such instances (in doubtful cases, the diagnosis might possibly be cleared up by means of venesection and the aseptic withdrawal of 1–2 c.c. of blood, for bacteriological examination). The post-mortem examination of the heart's blood has not as much diagnostic value as the examination during life. I must, therefore, take issue with those writers who align under the category of sepsis all cases in which bacteria (especially bacillus coli communis) have been found in the heart's blood after a long death agony. Even less ground exists for the opinion that all cases of melæna are due to sepsis.

Although the presence of the above-mentioned maladies is not precluded by the absence of evidence for their presence, still search must then be directed elsewhere for the cause of the hæmorrhage. The local diseases of the abdomen and its viscera must be taken into consideration, as must also the duration of the labor and the condition of the child post partum. A prolonged labor might have given rise to a cerebral hæmorrhage. At times much may be learned from the condition of the fontanelles; a bulging of the fontanelles with convulsions suggests meningeal or cerebral hæmorrhage. Lumbar puncture, in case there be a justifiable suspicion, may occasionally confirm the diagnosis. Asphyxia has occurred in only a small percentage of the observed cases (9 per cent. Silbermann). A careful history in reference to asphyxia neonatorum must be elicited, since this can undoubtedly give rise to hæmorrhages. A careful examination of the chest and observation of the respiration will determine atelectasis or congenital cardiac defects.

The *age of the child* at the time of the onset is of diagnostic value. It is highly improbable that sepsis is responsible for the hæmorrhage in case it begins immediately or shortly after parturition and no evidence is at hand for the existence of a congenital infection or an infection acquired during birth. On the other hand, the diagnosis of sepsis is highly probable when the bleeding starts after the fourth day of life. Hæmorrhages occurring in the second week of life or later (Ritter saw such cases occurring as late as the second month) may well be regularly laid at the door of sepsis.

The presence, in the stool, of large quantities of only slightly altered blood, is of diagnostic import, since in such cases spurious melæna is less probable than in cases in which comparatively small amounts of blood are vomited.

There still remain some cases, however, which in spite of the most thorough investigation are explained by neither the clinical examination nor the post-mortem findings (at the necropsy careful attention must be paid to the nose and brain and to blood infection).

The **prognosis** of gastro-intestinal hæmorrhage varies with that of underlying disease. Silbermann estimates the average mortality to be 44 per cent.; in individual cases, where organic disease can be excluded, the prognosis becomes more favorable the less blood the child loses.

Individual experience is hardly adequate in this connection, since melæna neonatorum is but rarely encountered. My own observations are limited to three cases; in two, sepsis was the cause and both terminated fatally; the third case, in which the cause was undiscoverable, made a complete recovery.

However the very numerous publications of later years, concerning the results of gelatine therapy, seem to promise a brighter prognosis. Since gelatine does not cure sepsis, the results of its therapeutic exhibi-

tion argue for the opinion that only a part of the cases of melæna are to be attributed to sepsis.

Treatment can, of course, avail in only a part of the cases of melæna. The best results have followed the use of gelatine. Merck's *absolutely sterile* (otherwise danger of tetanus) 10 per cent. gelatine is injected subcutaneously, under aseptic precautions, 10–25 c.c. (2–6 drams) and possibly 2–3 times daily. The needle wound is covered with gauze and sealed with adhesive or collodion. At the same time gelatine may be given by the mouth, in a 2–5 per cent. solution, a teaspoonful hourly or 25–50 c.c. (1–2 ounces) per rectum. Formerly, liquor ferri sesquichlorati (P. G.) in ½ per cent. mucilaginous solution (one teaspoonful hourly, or fluid extract of ergot, 0.25 c.c. (♏ 4) in two ounces of water, one teaspoonful every hour were recommended. In place of the last-named drug, ergotin may be used subcutaneously. Because of the rapid fall of the body temperature, the children should be wrapped in absorbent cotton and flannels and kept warm by means of thermophores and hot bottles (not applied to the abdomen, but best to the lower extremities). Local applications of cold are not to be used. The administration of small quantities of tea or the subcutaneous injection of physiological salt solution is recommended to support the heart, when large quantities of blood have been lost.

In cases of spurious melæna, the source of the bleeding, if accessible, is to receive appropriate treatment.

PREMATURITY AND CONGENITAL DEBILITY

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Prematurity and congenital debility are often looked upon as synonymous terms. However, it is apparent from the very meaning of the words that this idea is false; the word prematurity (partus præmaturus) means only, birth before term, whereas the expression debility (debilitas vitæ) is qualitative, in the sense that the respective child is deficient, compared with a healthy newborn infant.

The confusion of terms is, however, apparently justified by the fact that premature children are often debilitated; which occurs when one and the same poison (*e.g.*, parental syphilis) is responsible for both the premature interruption of pregnancy and the damage to the infantile organism. These constitute the diseased, debilitated, premature infants, on the one side of whom we can place the healthy premature infants, and on the other side, the debilitated full-term infants. Tarnier speaks truly when he says "not all premature children are weaklings and not all weaklings are premature."

It will, in the future, in accordance with the increase of our knowledge of these topics, be necessary to treat these conditions separately. At present, in view of the existing literature and in accordance with the practical purpose of this manual, this hardly seems feasible and moreover would lead to rather needless repetition. Utility, therefore, impels us to adhere, in the following, to a consideration of these themes—prematurity and congenital debility—in common; their principal points of variance will be succinctly emphasized in the separate subdivisions.

Although the term, prematurity, needs no further explanation, the expression, debility, requires exacter definition. Billard characterized it as a condition lying between health and disease. Very little is known of the anatomical changes or metabolic anomalies which are at the bottom of this status "*débilité congénitale.*" It is characterized by a quantitatively and qualitatively deficient vital energy and a lowered resistance to all infections.

Occurrence.—As shown by the statistics of lying-in institutions, premature children constitute a formidable percentage of the total number of births. The percentage varies widely with the locality and

the country; thus the number of children under 2500 Gm. (5½ lbs.) in weight and less than 45 cm. in length were:

In Moscow (orphan asylum) 5 per cent. (*Miller*).
In Munich (maternity) 13.3 per cent. (*von Winckel*).
In Halle (maternity) 25 per cent. (*Fehling*).
In Paris (Clinique Tarnier) 10.7 per cent. (*Budin*).
In Paris (Maternité and Clinique Bandelocque) 15.4 per cent. (*Pinard*).

It is stated that the percentage of premature births increases in the spring months, sinks during the autumn and is larger in winter than in summer.

Etiology.—Many causes exist for the occurrence of prematurity and they differ widely in their importance.

Thus external influences, such as severe physical exhaustion, mountain climbing, the lifting of heavy objects, traumata of various sorts, premature rupture of the fœtal membranes, etc., can furnish the impetus for premature labor. Twin pregnancy is also a frequent etiological factor. In 3380 plural births, Miller observed no less than 2040 premature children, that is 60 per cent. with a weight less than 2500 Gm. (5½ lbs.) and a body length under 45 cm.; Bachimont found in super-impregnated women, who were unable to take adequate rest, that the duration of pregnancy was shortened, on the average, by 22 days and the weight of the children brought down to 1900–1935 Gm. It is at present impossible to say to what extent faulty nutrition and physical excesses as well as psychic alterations in the mother, act in producing partus præmaturus. Maternal diseases play an important rôle in the etiology of both prematurity and congenital debility. Foremost in this connection is syphilis—and this ex patre as well—which, by extension to the fœtus affects its development and leads to partus immaturus or præmaturus. Other maternal diseases which lead to the premature expulsion of the fœtus are overshadowed in importance by the last-mentioned cause; these other diseases are: nephritis, heart disease and tuberculosis. Of the acute infections, scarlet fever is rightly the most dreaded. Prematurity is said to occur in two-thirds of the cases of pneumonia and to increase in probability with advancing pregnancy. Its occurrence with influenza depends upon the severity of the attack. The influence of malaria has been variously estimated, although with it, the spleen of the newborn infant can be enlarged. According to Voigt, prematurity occurs with variola in about one-half the cases befalling mothers vaccinated in girlhood. Measles, typhoid, bubonic plague, and Asiatic cholera can likewise give the impetus for a premature expulsion of the fœtus; and gonorrhœa more frequently than was formerly assumed. Endometritis leads to abortion more often than prematurity. Besides acute and chronic alcoholism, which are particularly prone to cause still-birth, there are various other poisons which produce intoxication of

both mother and child and can give rise to miscarriage or prematurity; these are especially phosphorus, arsenic, mercury, and lead. Typical signs of lead poisoning have been observed in a premature child.

Physiology and Pathology.—The weight of the premature child depends, on the one hand, on its age, on the other, on the cause of the premature labor. The extremes vary between 750 Gm. (1⅝ lbs.) and 3000 Gm. (6½ lbs.). According to Ahlfeld and Hecker, the averages of body weight and length in round numbers, are as follows:

Age.	Weight.	Length.
27 weeks	1140 Gm. 2½ lbs.	36.3 cm. 14 in.
29 weeks	1575 Gm. 3 lbs.	39.6 cm. 15½ in.
31 weeks	1975 Gm. 4½ lbs.	42.7 cm. 16½ in.
33 weeks	2100 Gm. 4¾ lbs.	43.9 cm. 17 in.
35 weeks	2750 Gm. 6 lbs.	47.3 cm. 18½ in.
37 weeks	2875 Gm. 6½ lbs.	48.3 cm. 19 in.

These figures have only an approximate worth, as can be seen from the following statistics of French writers, showing the widely varying weights of premature infants.

27 weeks.	29 weeks.	31 weeks.	33 weeks.	35 weeks.	Author.
1146 Gm. 2¼ lbs.	1540 Gm. 3 lbs.	1881 Gm. 3¾ lbs.	2213 Gm. 4⅜ lbs.	2400 Gm. 5 lbs.	François
1408 Gm. 2¾ lbs.	1700 Gm. 3½ lbs.	1900 Gm. 3¾ lbs.	2150 Gm. 4⅛ lbs.	.....	Potel
995 Gm. 2⅛ lbs.	1676 Gm. 3½ lbs.	1964 Gm. 3⅞ lbs.	2182 Gm. 4⅛ lbs.	2700 Gm. 5⅜ lbs.	Hahn

In case the average weight is less than that of a healthy fœtus of the corresponding age, it is justifiable to conclude that a greater or less number of these observed children were debilitated or at least ill.

In every case one must bear in mind that the weight especially, (even more so than the body length) is individually extremely variable; thus we have a type of children, usually from parents of slight stature, who are small in structure, and although they weigh only 2000 Gm. (4½ lbs.) they are in no way debilitated and show no signs of prematurity. According to Pinard, we find placentæ of very small weight with such children.

It is otherwise with hereditary syphilis in which strikingly large placentæ are found with the tiniest weaklings. The children of albuminuric and nephritic mothers are also small and puny and have been termed "spiders" by Pinard. The statistics of Berthod demonstrate how inadequate an aid the weight of the premature is for determining its age; these statistics include 48 children born at eight months or more, weighing less than 2000 Gm. (4½ lbs.) and among these seven full-term infants; also fifty-two infants born at less than eight months whose weight was more than 2000 Gm. (4½ lbs.), and among these two born at six months. The body length may be taken as a reliable criterion.

Body Temperature and Energy Balance.—Uncommon sensitiveness to low temperatures is peculiar to premature children and

weaklings. The temperature of a healthy newborn infant falls a few tenths of a degree centigrade after birth, but ordinarily soon returns to normal. This is not the case with the premature, and especially not, with the debilitated premature child. In these cases the temperature falls steadily to 32° C. (90° F.) and even lower, unless the child is placed in an especially favorable environment. On an average the less the weight of the child and the more debilitated it is, the lower its temperature. The reasons for this lasting hypothermia—whether a primarily deficient oxidation (Bonniot) or an inactivity of the thermo-regulative apparatus (nervous influence) as certain French authors are inclined to assume—remain unsettled.

After the initial drop, the temperature curve takes the form of a parabola. The longer the child is without artificial heat, the flatter the curve. A retarded rise, when in the incubator, is an unfavorable sign, just so an abrupt rise after a previously stationary, subnormal temperature. Also, premature children characteristically show an instability of body temperature in contrast to the slight nocturnal variations of the healthy young nursling. A deficient thermal regulation, which according to Babák is characteristic of all newborn infants, is found in an exaggerated degree in premature, debilitated children. Much energy is lost through increased loss of heat through the skin, on account of the relatively greater body surface of the premature child which also lacks adipose tissue. Added to this, these children lack, as do all newborn infants, the physical thermo-regulative capacity; whereas the chemical thermal regulation (increase in oxidation processes), which, in these children and especially the debilitated ones, is, without this, at a very low point, becomes taxed beyond its capacity. This leads to changes in the alkalinity of the blood (lowered to one-quarter the normal) and to the deposition of waste products and toxins in the body (Charrin, Guillemonat, Levaditi). Pfaundler, examining debilitated premature children, found the actual reaction of the blood to be acid. (The concentration of the OH–ions smaller than that of the H-ions.)

A more favorable balance of energy, showing a certain excess of energy necessary for increase in size and weight, is only possible by lowering the loss of heat by wrapping the child in a non-conductor of heat, by hot-water bottles or by raising the temperature of the environment—the use of the incubator. When one considers the difficulty of nourishing premature children, and their deficient assimilation, it becomes plain that the balance of energy very readily becomes negative; that is, the child loses ground. More exact knowledge concerning the dynamic exchange in premature or debilitated children is not at hand.

Behavior of Weight and Further Development.—The initial loss of weight is, according to the investigations of Déléstre and the writer, less than in full-term children. It depends on the quantity of

meconium, on the feeding, especially the ingestion of water, and on external circumstances. The separation of the cord plays no part in this connection. The gain in weight is, at first, despite sufficient feeding, slower than in the normal child, however it sometimes attains the average, after reaching the normal time of the termination of labor. The further development of the muscular and osseous systems, and of the teeth, and, finally, of the psychic functions, is, in healthy premature infants, backwards about the extent of time that the children are born prematurely. Czerny and Keller certainly speak truly when they assert that these children in later infancy are hardly to be recognized from full-term infants. Debilitated and sick premature children, on the contrary, often remain for years behind their contemporaries.

Special Pathology of the Organs.—The organs of unhealthy premature children are in a state of insufficient development; functionally they are usually backward and quantitatively deficient. In debilitated children we may have, in addition to the signs of prematurity, other physiological changes, causing qualitative deviation from the normal; these may or may not, depending upon the organ affected, be a menace to the life and impair the future development of the affected child.

The Nervous System.—In contrast to the healthy newborn infant the sleep of the premature child is even and deep and after lasting some time does not become lighter. Besides the somnolence, the indolence of the child's movements and the absence of all reactions are noticeable. The intelligence and psychic function develop more slowly—a fact which possibly depends on the insufficient development of certain centres.

Spasmophilia, as it has been described by certain writers, is not characteristic of premature children. Spasms, which occur immediately after birth, are not uncommonly the results of birth injuries. Intracranial hæmorrhages and cerebral diseases are especially apt to occur in small, first-born, premature children, according to Wallich. Premature infants, in fact, have a predisposition to nervous affections. Thus prematurity plays a prominent rôle in the etiology of Little's disease. Among 100 such cases Audebert found 82 in premature children. According to French writers, conditions of psychic depression and paralysis in childhood are found with relatively great frequency in premature children. Just how far hereditary syphilis is involved in these affections of the nervous system remains unsettled; however, it is certain that many an instance of cerebral atrophy is only the sequelum of a fœtal encephalitis.

Circulatory Apparatus.—The heart is comparatively strong; however cardiac weakness sometimes causes cyanosis and œdema (C. Hahn).

In a case of prematurity under my observation, I was able to satisfy myself that atelectases, by increasing the resistance in the lesser

circulation, can exert a retarding influence on and even entirely interfere with the physiological closure of the foramen ovale and ductus Botalli.

The fragile, brittle condition of the arterial wall in these children may have a connection with syphilis (mesarteritis syphilitica, Heubner).

The blood of premature children shows a deficient coagulability; there is a great tendency to hæmorrhages, especially epistaxis, and also melæna (sepsis?). In young premature children one finds nucleated red cells. Déléstre found that these forms disappear when the temperature of the child rises; they reappear, however, with any illness of the child. Leucocytosis was only present in slight degree. The decrease in the alkalinity of the blood has already been mentioned. According to Adriance, the percentage of hæmoglobin is excessively high, however, it gives way soon after birth to an increased destruction of cells; this fact probably has some connection with the occurrence of icterus, the non-syphilitic forms as well, in these children.

The lymphatic apparatus shows in contrast to the full-term child, a noteworthy anatomical completeness; however, owing to the slowness of its circulation, it probably more easily permits of the escape of toxins and bacteria.

The Respiratory Apparatus.—The breathing of little premature children is shallow and irregular. The voice is monotonous and feeble. On auscultation one can barely hear the vesicular respiratory murmur. The percussion note is flattened toward the bases. Not uncommonly, on account of the diminished respiratory excursion, the lower parts of the lungs remains in a condition of atelectasis; the air does not reach the alveoli, but only the finer bronchi; this explains the predisposition to pneumonia that exists in these children. Accompanying this we have, as especially important in the pathology of the premature child, attacks of cyanosis and asphyxia which occur soon after birth, on account of pulmonary atelectasis.

These attacks often occur without warning in well-developed children, the face and hands becoming cyanotic. Respiratory pauses, one or more minutes in duration, recur so that the breathing resembles the Cheyne–Stokes type. Convulsions are also observed. The pulse is greatly slowed-down to 40 beats per minute or less.

The cause of these attacks is not clearly established. Finkelstein believes them to be the consequence of a subtly developing carbonic-acid intoxication, which is brought about by insufficient breathing or also by meteorismus and the consequent encroachment upon the intrathoracic capacity.

Budin considers them to be the consequence of chronic underfeeding and sees them disappear with the institution of forced feeding. From several personal observations, I have gained the impression that they are cerebral in origin, but cannot substantiate this belief with

autopsy findings. Occasionally the attacks seem to be elicited by the feeding of the child.

Billard and, after him, other writers have described a condition in the premature child, with which respiration is entirely wanting. The heart's action is weak and slowed. The blood flows from the right heart through the ductus Botalli into the aortic system without ever passing through the lungs. In this manner a *"vita minima"* can be maintained for a few days; such observations, however, belong to the rarities and are without practical importance.

The Digestive Tract.—Marfan considers the digestive tract to be the most vulnerable "organ-system" of the premature child; still the difficulties can usually be overcome through a properly instituted feeding. Small premature children are incapable of suckling and even larger ones are thereby easily exhausted. Swallowing is slowed. The digestive fluids (ferments) are quantitatively and qualitatively deficient as compared with the normal, although exact researches concerning this are not at hand. French authors write of functional disturbances of the liver in weaklings. The meconium, which is usually scant, is delayed in its passage; likewise one often encounters, in the first weeks, a constipation or rather pseudo-constipation which is the result of diminished intestinal activity or underfeeding.

Finkelstein has repeatedly observed an atrophy of the stomach occurring in the later months and this justifies his warning against the overfeeding of premature infants.

Skin and Adnexa.—The skin is more or less intensely reddened and covered with lanugo hairs; the redness persists somewhat longer than with full-term children; the external ears lie, as foldless skin-tabs, close against the skull; the nails are either absent or else fall short of the end of the phalanges; the insertion of the umbilical cord lies deeper than normal, and the epidermal desquamation is slowed. Owing to the absence of the adipose layer in the subcutaneous cellular tissue, the skin lies loose and movable over the underlying parts. Erosions occur easily after the slightest injuries; these losses of substance occur especially over the malleoli and the heels. Besides sclerema and sclerœdema, to which these children are very prone, there occurs a form of icthyosis described by French authors, concerning which, however, nothing definite is known.

The Kidneys.—The frequent occurrence of uric acid infarctions is explicable through the deficient oxidation and the insufficient circulation and respiration; the ingestion of too small a quantity of water may also have something to do with this. Uric acid infarction can give rise to a suppression of urine lasting for one or more days, which in turn occasionally leads to colicky and convulsive states (encephalopathie urémique, Parrot).

Baumel cites a case ending in recovery, in which a premature child urinated through the umbilicus (urachus). According to Charrin the quantity of urine is low and the acidity and toxicity are raised.

The proportion of ammonium N to total N is less than the normal; $\frac{C}{N}$ on the contrary is increased, which points to an increase in the decomposition processes. According to Nobécourt and Lemaire, a lowering of the freezing point ($\triangle$) of the urine of premature infants is likewise present.

Herniæ, especially umbilical herniæ, occur with relative frequency in premature children.

The bacterial infections, which can occur intra-uterine, intra-partum, or extra-uterine, play a weighty and characteristic part in the pathology of the premature child.

The extra-uterine infections, which usually lead rapidly to death, can take place through the skin, the mucous membranes, the respiratory tract, the eyes, mouth, intestinal tract, and navel. According to Fischl and Déléstre, with whom I herein agree, the lungs afford, especially in hospital patients, the most frequent point of entry for bacterial invasion; in this connection, a subnormal body temperature furnishes a predisposing element. These children usually die within a few days, of a hæmorrhagic form of pneumonia, occurring under the clinical picture of asphyxia, usually running an afebrile course. Déléstre found coryza occurring only in premature children with a normal temperature.

Henry describes a rhinitis, running a chronic course in premature children, which, contrary to the associated assumption, is not specific.

Diagnosis.—The diagnosis of prematurity is made, in extreme cases, from the typical general appearance. Besides the small size, the characteristic signs of unripeness strike the eye.

The most important clews, besides the duration of the pregnancy, are furnished by the weight and measurement of the child.

Fewer external characteristics come into consideration for the diagnosis of debility.

A low body weight—under 2500 Gm. (5½ lbs.) (Czerny and Keller) can, as these authors themselves declare, hardly be considered as a sharp boundary. It is rather the general behavior of the child, a diminished resistance to external harmful influences (temperature, infection, artificial feeding, etc.), which inform us, often not until weeks after the birth, that we are dealing with a debilitated child.

Prognosis.—The prognosis of a premature child depends first and foremost on its absolute age, which is its degree of ripeness. A child which is born before the twenty-seventh to twenty-eighth week of pregnancy has only a small chance of remaining alive.

The weight takes second place as an indicator, and therefore a small older child is better off than a large younger one. Notwith-

standing this, statistics rightly show a decrease in the mortality with increasing natal weight. It is palpably clear that a child weighing 1800 Gm. (4 lbs.), other things being equal, has better chances than another weighing 1200 Gm. (2½ lbs.); then again, the heavier child can have a worse prognosis, provided it be not only premature but also at the same time debilitated.

Hereditary influences: parental diseases, especially maternal (syphilis, tuberculosis), are very important for determining the capacity for life of the little neonate. When the premature birth is artificially induced, because of some mechanical reason (contracted maternal pelvis) the prognosis is naturally better.

According to Budin, children having a rectal temperature of 32° C. (90° F.) and less, die almost uniformly. The behavior of the child immediately after delivery is very important prognostically. Children that cry lustily, move in a lively fashion, drink well, or even suck of their own accord on the proffered breast, have much better prospects than those children, apathetic, hungry, and cold, with temperatures of hardly 32° C. (90° F.) that are not given medical attention until days after birth.

Although the prognosis at first is dubious, it later becomes better in proportion as the care and nutrition are entirely satisfactory, and complications do not occur.

Mortality.—Potel's statistics show the influence of the absolute age in the mortality.

Of 56 children of 6½ fœtal months	.45	= 80.4 per cent. died
Of 131 children of 7 fœtal months	.76	= 58.1 per cent. died
Of 53 children of 7½ fœtal months	.17	= 30.1 per cent. died
Of 110 children of 8 fœtal months	.39	= 35.5 per cent. died

Credé established a mortality of 83 per cent. for children weighing 1000–1500 Gm. (2½–3 lbs.); a mortality of 36 per cent. for those weighing 1500–2000 Gm. (3–4½ lbs.); and 11 per cent. for those weighing 2000–2500 Gm. (4½–5½ lbs.).

In these statistics, however, one must remember that the healthy and debilitated premature children are not separated. Francois separated these two classes and arrived at the fact that of 81 premature children of diseased parents (syphilis, tuberculosis, albuminuria) 30 to 37 per cent. died; whereas of 386 approximately healthy premature children, only 48 (12.5 per cent.) died. Just how much can be done, even in institutions, in the way of decreasing the mortality rate of premature children, is shown by the publications of Hutinel and Déléstre, who were enabled to reduce the death rate from 66 per cent. to 36 per cent. and later to 14 per cent., "thanks to the almost motherly care, the isolation of the sick, the use of the conveuse, the mother's milk and a sort of air-cure."

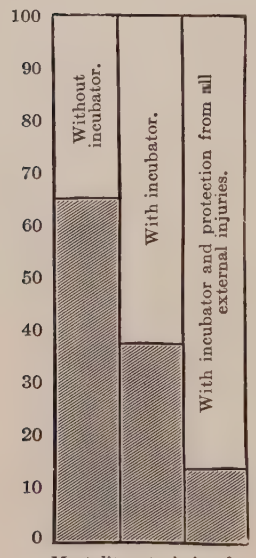
According to Groth of Munich, the mortality from congenital debility during the first month of life, is lowest in August and highest in the winter months.

Aside from the first two weeks, the mortality of premature children is hardly higher than that of healthy full-term ones.

According to Budin, 15 per cent. of the premature children died after discharge from his institution and 17.4 per cent. of the full-term ones, after discharge.

Pathological Anatomy.—Post-mortem examination of young premature children distinctly discloses their unripeness, besides an anæmia of the organs. The organs correspond to the fœtal development. The lungs are very anæmic and show either partial or total atelectasis. The brain, of colloid consistency, permits only of inaccurate differentiation into white and gray substance, the gyri are imperfectly developed, the pyramidal tracts in the spinal cord are still undeveloped. The kidneys plainly show renculin formation. The thymus, thyroid, and adrenal are noticeably large. The fœtal channels (ductus Botalli, ductus Arantii, and foramen ovale) are still open, showing insufficient involution. The epiphyseal osteogenetic centres are very small and undeveloped. In syphilitic premature children, besides other specific manifestations, one finds the osteochondritis of Wegner (see chapter on syphilis).

Fig. 10.



Mortality statistics for premature infants.

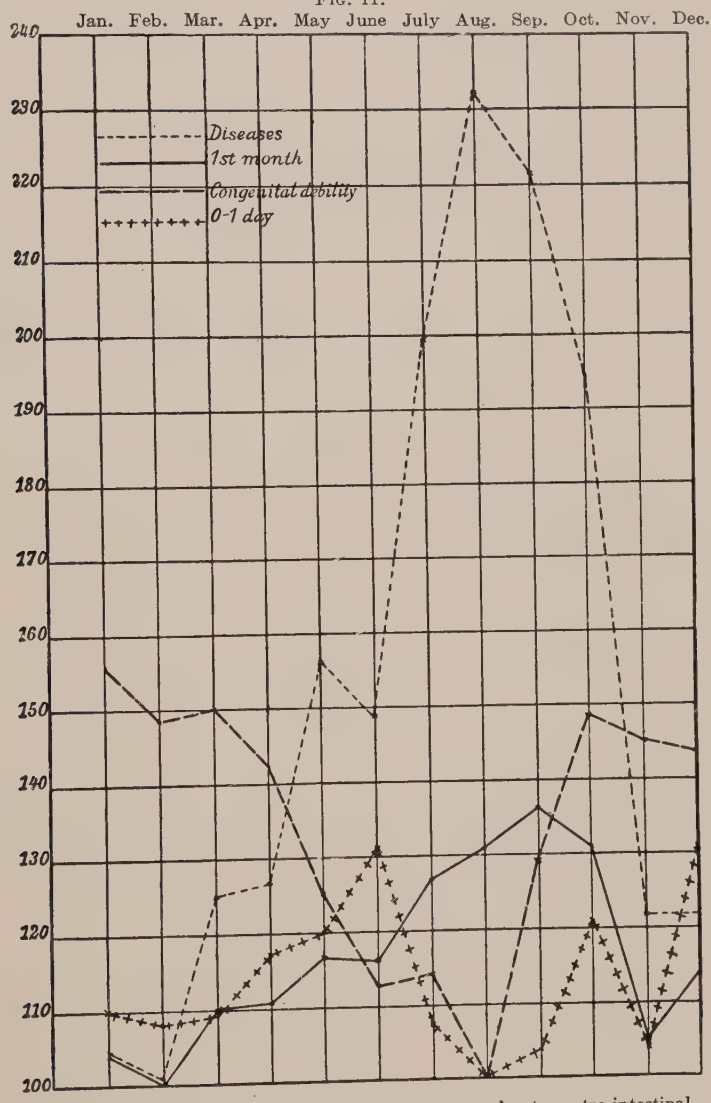
Prophylaxis.—The prophylaxis is a twofold one. In so far as it concerns the occurrence of a premature birth, it does not come within the range of this book but rather belongs to the province of the obstetrician or syphilographer. The prophylaxis of the premature child consists in keeping away all external harmful influences; in its positive phase it is curative, in the furnishing of skilled care, warmth and natural food.

Treatment.—The treatment of premature and debilitated children consists (1) in the furnishing of warmth; (2) in careful feeding; and (3) in the avoidance of harmful influences, particularly bacterial. Other measures, especially medicinal, are of much less importance.

1. Furnishing warmth to the body, immediately after birth, is, according to the unanimous opinion of all authors on this subject, the first and most important measure in the treatment of the premature child. A bath of 37° C. (98.6° F.) increased to 40° C. (104° F.), and the careful transportation of the infant into a previously prepared warm room, most surely secure this. A bath of the above-given temperature

lasting fifteen to twenty minutes is also the best measure to quickly bring the fallen temperature back to normal, in children that only come under treatment later. Eröss rightly states that not all premature children require artificial warming. However, the small and the debili-

FIG. 11.



Compare extreme height of the mortality in summer, due to gastro-intestinal diseases, with the zero of the deaths from debility in August.

(Course of the mortality in the first month of life, in Munich. Separated according to cause of death.)

tated ones do require it in one or another form. The supply of heat should be accurately measured for it has distinct indications and contraindications. In case the three hourly rectal temperatures show a subnormal temperature, artificial warming is demanded. Whereas in

private practice one usually must get along with crude appliances, in maternity hospitals and clinics for nurslings one usually finds apparatus for furnishing warmth (incubators), which with advancing improvement and decreasing cost will be in the near future more widely used in private houses.

The principal requisites of an incubator are (1) simplicity and surety in working, (2) cleanliness, (3) artificial light, ventilation and moistened air*, (4) accurate regulation of the temperature, that is, dosage of the supply of heat. We must admit unfortunately that despite the greatest care there is hardly an existing model which fulfils all these demands.

Although the problem of the therapy of the premature is in no way fully solved by furnishing a good incubator, and even though its use be confined to those cases where a strict indication is at hand, still the results obtained from its employment are so convincing (compare Berthod, Gagey and others), that the greatest possible perfection in such apparatus seems well worth while.

The opponents of the incubator may content themselves with the dictum of Délestre, who says, "Tant vaut le milieu, tant vaut la couveuse."

I will omit the historical description of the various models.

An apparatus which is a modification of the French model devised by Finkelstein (Fig. 12), and in use in the City Children's Asylum of Berlin, appears to be both practical and simple. It is made of galvanized steel tin, with rounded edges. The box, which rests on a stand, is divided into two parts; an upper compartment, partly of glass, which is the receptacle for the child; and a lower compartment, the hot water receptacle, closed by means of a sliding panel. Cold air enters through openings located on the side of the lower part, is there heated, and then passes through the upper compartment, leaving it by means of the air vent. The necessity of regularly changing the hot water containers, makes punctual attendance imperative.

The author's incubator (Fig. 13) with its latest improvements, can, similarly, be erected very cheaply in either house or clinic. It is divided into a compartment for the child; the heat and moisture generator; a water container and heat box. The accompanying diagram makes a detailed description unnecessary. The cubic contents of the incubator is 0.09 cbm., and 4.97 cbm. of air pass through it in the course of an hour, consequently the air changes fifty times hourly.

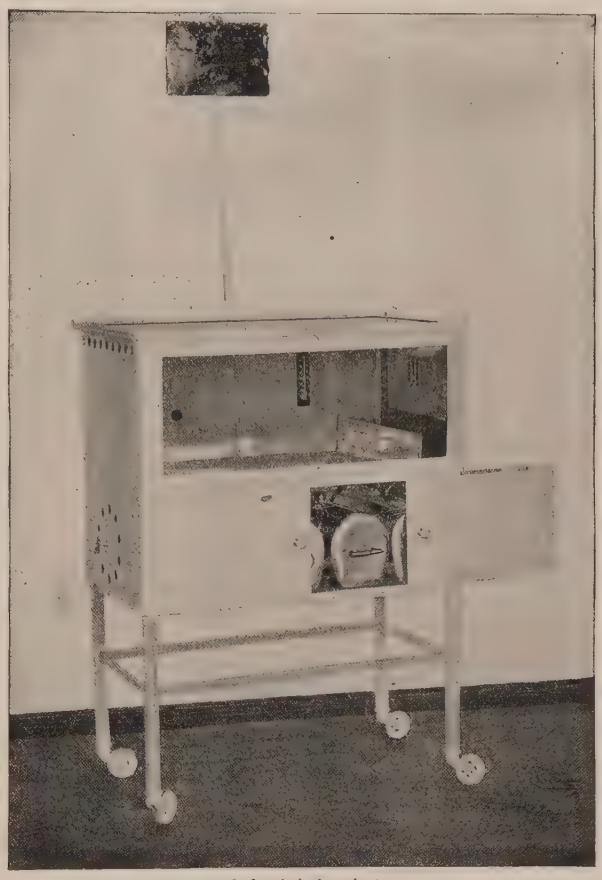
Besides Schlossmann's electric heated incubator, the one of Hutinel also deserves mention. In view of the danger of infection which has often been attributed to the conveuse, the latter is made of varnished

* The quantity of air should be 1.5 cm. an hour for each kilogram in weight of the child. The humidity should be about 60 per cent.

fayence, shaped like a bath tub. The rest of the apparatus is very similar to the Finkelstein one; the heating appliance being changed every two to three hours.

Several institutions (Children's Hospital, Gratz, St. Anna Children's Hospital, Vienna, and elsewhere) have incubator rooms (see Fig. 14). These are far superior to the simple incubators and according to the judgment of experienced clinicians are well adapted for use in institutions; they can even at times be improvised in private practice, if one has an abundant supply of heaters at command.

Fig. 12.



Finkelstein's incubator.

The room in which a premature child is kept, with or without a couveuse, should be of an even temperature, from about 22°–25° C. (71.5°–77° F.), and should conform to the inexpensive requirements of modern hygiene, at least as far as cleanliness, ventilation, and sunshine are concerned. The air in the room should be kept sufficiently moist. The temperature in the incubator must be kept from 26°–28° C. (79°–82° F.), at the start; only very small, premature children require a higher temperature. It hardly seems practical to keep the temperature of the incubator constant, at 25° C. (77° F.) as recommended by Pinard.

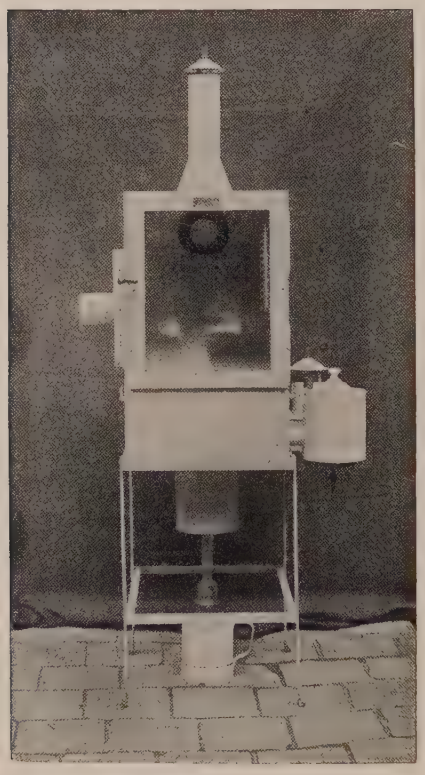
If the body temperature is not raised by the above-mentioned temperature of the incubator, the humidity of the air must be increased by placing hot, moist towels in the incubator—"couveuse humide" recommended by von Bonnaire and Gagey, by means of which these authors have attained surprising results.

With the slightest signs of overheating (restlessness, sweating,

increased respiration, cyanosis) the body temperature must be reduced, if necessary by removing the child from the incubator.

Hutinel and Deléstre make use of the incubator for as short a time as possible, and after maintaining an even temperature from one to two days, recommend the removal of the child from the incubator. Likewise, every acute infection furnishes a contraindication to the use of the incubator. One can use as a substitute for the incubator treatment, heated tubs, hot water bottles, thermophores in the form of heat-pillows (highly praised by Heubner), as well as the electro-thermostat lately put on the market.

Fig. 13.



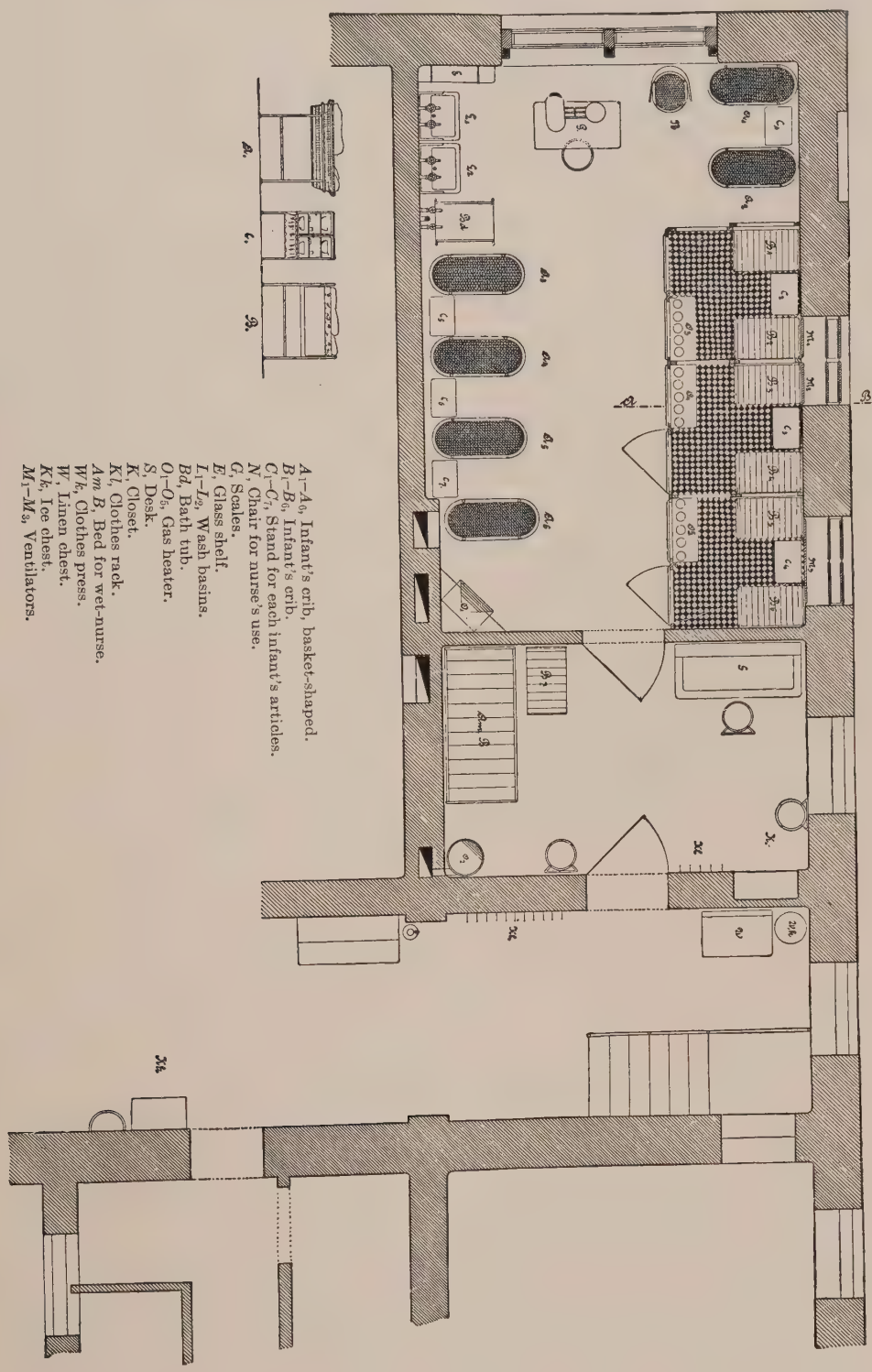
Rommel's incubator.

In using the above-given methods, the breathing air does not become heated, while, on the other hand, an over-heating of the child, by insufficient radiation of the heat, can readily take place. Nevertheless, the simplest way is by placing two to four hot water bottles in the bed which must be refilled every two hours. The rectal temperature must be taken regularly so that any stasis of heat, which may cause serious trouble, can be detected.

The U-shaped hot water bottle, which appears in the accompanying illustration Fig. 15, has proved itself very useful because frequent refilling is unnecessary.

2. *Feeding* and its technique are particularly important in the therapy of premature and debilitated children. Above all things mother's milk is desirable. It must be considered a grave error, if, through any negligence, the opportunity to obtain mother's milk is lightly passed by. This applies in a still greater degree for debilitated children (especially with hereditary syphilis), whose prognosis actually depends on their being nursed at the breast (Heubner).

The greatest difficulty is the inability of the premature child to nurse and in private residences it is especially a very difficult task to accustom the child to the breast; in primiparæ with poorly secreting breasts or retracted nipples, this is next to impossible. Only the greatest patience in expressing and pumping the milk by means of a strong breast-pump, to avoid caking, or still better, the comcomitant nurs-



A_1–A_6, Infant's crib, basket-shaped.
B_1–B_6, Infant's crib.
C_1–C_7, Stand for each infant's articles.
N, Chair for nurse's use.
G, Scales.
E, Glass shelf.
L_1–L_2, Wash basins.
Bd, Bath tub.
O_1–O_5, Gas heater.
S, Desk.
K, Closet.
Kl, Clothes rack.
Am B, Bed for wet-nurse.
Wk, Clothes press.
W, Linen chest.
Ke, Ice chest.
M_1–M_3, Ventilators.

FIG. 14.

ing of a stronger, older infant, will bring the breast into operation. With this purpose in view, it is advisable to place both mother and child in a nursling's home, or some similar institution. Wet-nurses advantageously continue nursing their own children along with their charge, thus keeping the milk supply up to the highest point. In selecting a wet-nurse for a premature child, the greatest care should be exercised to detect the possible existence of a latent syphilis. Occasionally a skilfully directed "allaitement mixte" accomplishes the desired result.

The child, thus strengthened, attacks the breast more vigorously and thereby increases the secretion of the mother's milk. It is of great importance to know the daily amount of nourishment necessary, and thereby avoid both overfeeding and underfeeding. Both are harmful. Nevertheless the greatest danger in practice seems to be the underfeeding of small premature children. They seem to require a relatively greater amount of food at this time than in the later nursing period. The volume of food each day to be determined by either the scale or graduate, for the first ten days of life equals V=n+10 (in c.c.; n= number of days) per 100 Gm. For example, a child weighing 1500 Gm. requires on the fifth day of life about 5+10=15 per cent. of the body weight, which equals 225 Gm. of mother's milk. Later a premature child should drink about one-fifth of its body weight per day, and at full term one-sixth.

Fig. 15.

U-shaped hot water bottle for premature infants.

The amount of energy, in this volume of food, required by a flourishing infant varies from 130–120–110 calories per kilo of body weight, diminishing with the increasing weight and age of the child.

Technique of Feeding.—As it is not possible to feed large quantities at a single meal to small premature infants (often only 10–20 Gm.; ℥iiss–℥v) it becomes necessary to nourish them every two hours or even at shorter intervals, *i.e.*, ten to twenty times in twenty-four hours. Czerny and Keller only give six, sometimes five meals in twenty-four hours. In feeding according to this schedule, it seems impossible to avoid underfeeding.

In very small premature infants the nourishment must be introduced (gavage) by means of a Nélaton catheter, or allowed to slowly trickle into the mouth or the nose by means of a pointed spoon. The

glass flasks depicted in the accompanying illustration Fig. 16 (Undine's) have proved very useful in oral and nasal feeding.

Before feeding, small premature infants must often be stimulated by means of slapping, pinching, etc. A short bath of 37°–39° C. (98.6°–102° F.), or a cool sponging is often useful. Many children immediately eject their nourishment and it requires great patience and skill on the part of the nurse to make them retain it.

The artificial feeding of premature and debilitated children will always come into account only as a last resort; the result will always be uncertain and it is difficult to recommend any one method. The formula must be controlled by the general condition and by the stools, and must resemble mother's milk as nearly as possible in amount and caloric value. Overfeeding with its harmful results must be strictly avoided in the artificial feeding of premature infants. Self-prepared whey—milk mixtures of 2:1 and 1:1; also milk diluted with an equal quantity of calf's broth, are indicated. There is a division of opinion as to the amount of cream necessary for premature infants. I have no experience with the butter-milk carbohydrate mixtures, lately recommended by Finkelstein. Budin and Michel praise a mixture in which the albumin has been peptonized by the action of a fresh extract of calf's pancreas. Although there are many references in the literature recommending peptonized milk for the feeding of premature infants, I cannot conscientiously recommend the use of the factory preparations of milk.

Fig. 16.

Feeding glass for premature infants. Can be used for nasal or mouth feeding.

The prevention of infection, of every sort, is most successfully accomplished by skilful attendance. The cord should be carefully dressed with hydrophilic gauze, moistened with 1–2000 bichloride solution. Cleansing the mouth should be omitted as it is useless and moreover harmful since the oral epithelium is very easily injured. The bath water should be boiled. Sponge baths with warm water and very fatty soap are preferable to tub baths at first. The new dusting powders, or talcum with the addition of boric acid 1:2, should be used. Ointments as a rule are very poorly tolerated. The customary clothing is used and should always be previously warmed; only very small premature infants should be wrapped in cotton. All chilling and the too early airing of the premature child are to be avoided.

Of the remaining therapeutic measures for premature and debilitated children, we will only mention the following:

The use of oxygen (Bonnaire and Geneay recommend its use as a prophylactic as well as in cyanosis, asphyxia, infections and vomiting).

Blood-letting. (Déléstre recommends repeated bleedings of 2–3 c.c. in children who do not gain sufficiently; also a single bleeding of a larger amount, 18–20 cm.).

Injections of artificial serum (20–30 c.c.) are also recommended by Déléstre and other French authors. Budin regards massage with hot oil, repeated 2–3 times daily as very useful.

Complications are to be treated accordingly.

ASPHYXIA AND ATELECTASIS

BY
DR. O. ROMMEL, OF MUNICH

TRANSLATED BY
DR. A. S. MASCHKE, CLEVELAND, O.

ASPHYXIA is a disease of the newborn, with which the interchange of gases of the blood—absorption of oxygen and elimination of carbon dioxide—is either suspended or more or less diminished. Through the diminished ventilation of the blood, a pathological oxygen-deficit ensues and an overloading with carbon dioxide, a condition of asphyxia, which seriously threatens life. If the respiration is utterly wanting one speaks of apparent death ("Scheintod").

We differentiate two forms of asphyxia:

I. *The congenital form,* usually beginning sub partum, and which occurs as (*a*) asphyxia cyanotica I degree, and (*b*) asphyxia pallida, II degree (Runge).

II. *The acquired form,* which occurs after birth and which on account of its usual clinical and pathological findings has also been termed atelectasis.

Both forms are to be sharply differentiated in respect to etiology, occurrence and course; this however does not prevent both forms from occasionally occurring in the same child or going over into one another.

I. CONGENITAL ASPHYXIA

The discussion of this form in this place will be short, since it really belongs to the province of the obstetrician.

Etiology.—The premature excitation of the respiratory centre, through which futile inspirations are elicted ante partum, can occur in many ways:

I. Causes on the part of the infant:
   (*a*) Compression or twisting of the umbilical cord.
   (*b*) Premature detachment of the placenta.
   (*c*) Abnormal cerebral pressure in the fœtus.

II. Causes on the part of the mother:
   (*a*) Insufficient maternal circulation and arterialization (especially with heart and lung affections).
   (*b*) Lowering of the maternal blood pressure on account of hæmorrhages, agony, death of the mother, labor.
   (*c*) Anomalous labor pains, *e.g.*, tetanus uteri.

With the increase in the carbon dioxide contents of the infantile blood, the irritability of the respiratory centre in the medulla decreases and severe paralysis of the respiratory function of the newborn can arise, through which the lungs can remain, even after birth, in the fœtal state of atelectasis.

Symptomatology and Course.—This asphyxia, arising intra utero from the above-mentioned causes, begins almost always shortly before birth, often develops rapidly and may become a serious menace to the life of the child.

Of the *symptoms* indicating intra-uterine asphyxia, besides the passing of meconium, the most reliable is the weakening of the fœtal heart sounds. This symptom, due to irritation of the vagus, gives place, in severer stages of the asphyxia, to a considerable increase in the heart sounds (vagus paralysis) and demands the immediate ending of the labor. The asphyctic newborn is cyanotic, varying in color from a bluish-red to a deep blue (asphyxia cyanotica first degree of Runge). It lies motionless with a swollen face and closed eyelids, its little legs slightly flexed. The breathing is superficial and infrequent and is accompanied often by rattling and hiccoughing. The heart's action is strong and usually infrequent. The muscular tone and also the reflex excitability are retained. Reflex choking movements are elicited on introducing the finger into the pharynx in order to aid in the removal of mucus. By irritating the skin, deeper inspirations are elicited which however usually soon diminish in intensity.

FIG. 17.

Pulmonary atelectasis in the newborn. The alveoli (1) are collectively collapsed. The interspaces (2) represent the alveolar ducts. (3) Transition of a bronchiole to an alveolar duct. (4) Cross-section of bronchus.

With the second degree (asphyxia pallida) the skin is pale, the lips alone are bluish, the muscular tone is wanting, all the extremities hang loosely relaxed, reflex irritability is lost and the heart's action is frequent and weak. Respiration is entirely stopped, at the most one observes here and there a jerky, almost convulsive, movement of the whole child. The upper air-passages are usually totally occluded and thus the entrance of air is hindered by mucus and amniotic fluid, aspirated in consequence of premature respiratory movement.

Gradually the heart's action ceases and the body temperature sinks and thus these children usually die; others occasionally drag on for a few days, but only to die. Where the treatment avails, respiratory movement starts, the eyes are opened and the child moves with increasing liveliness. The skin becomes rosy and feels warm, the pulse strong and regular, mucus is expectorated (vomited) for days.

Pathological Anatomy.—The signs of death from asphyxia are most evident: thin, watery blood; the right ventricle and the large vessels distended, as also the veins leading from the brain and liver; the liver is dark blue in color; petechial and larger hæmorrhages under the pleura, pericardium, peritoneal covering of the liver, the pia and other organs; also hæmorrhagic-serous effusions into the pleural, pericardial and peritoneal cavities.

Besides this are the signs of attempts at respiration before delivery; congestive hyperæmia of the lungs; ecchymoses under the pleura and pericardium. The respiratory passage (larynx and bronchi) is filled with mucus, amniotic fluid or meconium and one can often trace these masses through to the finer bronchi.

In children who are born asphyctic but have lived, one finds, besides the more or less extensive atelectases, also air-containing areas; the latter much lighter in color and raised above the atelectatic areas; the atelectases dark and leathery. Amniotic fluid and meconium are not rarely found in the stomach since swallowing movements may occur with the attempts at ante-natal respiration.

Diagnosis.—The diagnosis of asphyxia is made from the clinical picture and doubt can also arise as to whether in a given case one has to do with a combination with cerebral compression or not; a not uncommon condition in first-born premature infants.

According to Runge the diagnosis of an asphyxia complicating cerebral compression is justifiable when, with an asphyxia of the first degree, the breathing continues irregular and more infrequent and the pulse rate diminishes in spite of the institution of energetic cutaneous stimuli. In case one suspects an acute anæmia search should be made for the cause of such an anæmia, *e.g.*, velamentous insertion of the cord.

Prognosis.—Unless skilful treatment is employed the prognosis is grave. Usually the asphyctic children of the first degree go over into the second degree, whereas the latter die. With suitable treatment the milder cases usually recover and even the severe cases are not entirely hopeless if peristent treatment be kept up.

The opinion advanced by Schultze and Jacobi concerning the appearance of a later idiocy, after severe and protracted asphyxia, and also the reports of Little and Mitchell which refer to the connection between birth trauma and nervous and psychic lesions, are not taken into consideration prognostically, in individual cases.

Prophylaxis.—This falls within the province of obstetrics.

Therapy.—The treatment of asphyxia neonatorum consists in the use of the following measures:

1. *In the Clearing out of the Air Passages.*—If mucus or amniotic fluid penetrate into the air passages, one must aspirate through a Nélaton catheter, steadily sucking while advancing the catheter. The method of Ahlfeldt and Pinard, which consists in suspending the child by its legs, for a quarter of a minute, thereby causing the congestive hyperæmia to act in the greatest degree on the respiratory centre, also seems practical. At the same time the mucus should be aspirated. Prochownick recommends rhythmic compression of the thorax while the child is in this suspended position.

2. *The Use of Active Cutaneous Irritants.*—Alternating hot and cold douches are most effective. The child is immersed to its neck alternately in warm water of 40° C. (104° F.) and cold water of 20° C. (68° F.). The treatment must always start and end with warm water immersions; besides this, the usual cutaneous irritations by slapping the gluteal region.

3. In every severe case of asphyxia (II degree), uninterrupted, *prolonged artificial respiration* must be employed. The writer considers Schultze's swinging method to be the most effective of all. In regard to the well-understood technique of this method*, we need only note that after six to eight swinging movements, the child should always be immersed in warm water of 38° C. (100° F.), in which one must employ thorough friction, and rapid rhythmical compression of the heart in order to raise the cardiac action to 120–140 a minute. The suspicion, recently raised, that Schultze's method might give rise to rupture of internal organs with consequent hæmorrhages, lacks sufficient proof. One should never despair of resuscitating the infant as long as any sign of cardiac action be present and restorative measures must be kept up until the child cries long and lustily (Schultze).

Sylvester's method of artificial respiration also deserves mention; it consists in the strenuous abduction and adduction of the arms and shoulders, thus increasing or decreasing the intra-thoracic capacity.

Laborde's method by traction on the tongue is difficult of execution in the newborn, on account of the smallness of the part to be manipulated.

The method of Pernice, consisting in the use of faradic electricity, has been abandoned, since by it only inspirations can be elicited. Contrariwise, however, the results from the use of oxygen have been rather gratifying.

II. ACQUIRED ASPHYXIA

This is also called atelectasis pulmonum and is encountered in premature and debilitated children. We differentiate according to the

*See text books on Obstetrics.

onset an early and a late form of asphyxia. (Concerning the latter see also the chapter on prematurity and debility).

The **etiology** of this form of asphyxia is rather complex.

I. General debility with which all the functions are quantitatively and qualitatively impaired and a high degree of somnolence exists; with this, through a lingering carbonic acid intoxication, paralysis of the respiratory centre results (Finkelstein).

II. Cerebral diseases; especially injuries in the region of the medulla, from birth-traumata (hæmorrhages?); also congenital hydrocephalus.

III. Pulmonary affections (aplasia of the lungs, white pneumonia); also congenital struma or hyperplasia of the thymus which leads to compression of the trachea.

IV. A yielding thoracic wall and costal cartilages, as well as a poorly developed respiratory musculature in premature children.

V. Acute fatty degeneration of the newborn (Buhl's disease) which in the absence of hæmorrhages can be masked through the symptom of asphyxia.

VI. Underfeeding (Budin) as well as overfeeding (Henry) are held responsible as etiological factors in cases of asphyxia in premature children.

The **course** of asphyxia occurring soon after birth, especially in premature and debilitated children, is usually as follows: the children usually slumber apathetically, without demanding nourishment, and are noticeably quiet. The face is at times slightly puffed and slight œdema occurs on the extremities, especially on the backs of hands and feet. The temperature is subnormal. The breathing, tolerable at first, becomes more superficial and irregular; now quicker and now interrupted by longer pauses. Ausculation, after having spanked the child a few times, reveals crepitant râles usually over the bases (atelectatic crepitations). In some children one observes localized lateral retractions, also at times in the middle of the sternum. Now and then severer attacks of cyanosis intervene without warning. With a falling temperature and marked loss of weight, the children die usually within a few days and often even within a few hours. Now and then the asphyxia occurs, especially in premature children, as late as a few weeks after birth and is then usually a very bad sign.

The **pathological anatomical findings** are often totally negative except for a more or less extensive pulmonary atelectasis.

The **diagnosis** is furnished by the pulmonary findings, the impairment of respiration, the increasing stupor and the poor appetite.

The **prognosis** depends, first, on the cause underlying the asphyxia. It depends further on the treatment instituted. Should any improvement of the condition be secured by means of the therapeutic measures,

one usually wins the battle. This, however, does not hold good for the cases of asphyxia occurring later in premature children, which usually terminate fatally.

The **treatment** of acquired asphyxia consists chiefly in the use of hydrotherapeutic measures. The alternating hot and cold baths recommended, under 2, for congenital asphyxia, often prove valuable when frequently repeated. Heubner recommends baths at 35° C. (95° F.) of only short duration, combined with pouring cold water 10–12° C. (50–53½° F.) over the chest, back and head four to six times, using one pint each time and repeating regularly every two hours. Besides this, warmth and breast-feeding. In these cases oxygen inhalations are especially recommended. The other therapeutic measures recommended for congenital asphyxia may also be symptomatically employed.

SCLERŒDEMA AND SCLEREMA

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BOTH these diseases, between which formerly no differentiation was attempted, have now obtained an assured place in the pathology of the newborn and the young nursling.

In the older literature a considerable confusion dominated the subject of these affections. The confusion with the scleroderma of adults* contributed in no way to the clearing of the situation. However, since the writings of Denis and Billard, most authors have sought to differentiate two forms, a serous and an adipose hardening of the skin. The "arbeit" of Clementowsky, which was grounded on accurate clinical and anatomical investigations, marks a noticeable advance in the knowledge of these diseases. And, although according to Luithlen no entire clarity exists to-day concerning these topics and discussion even exists in the text books, still this does not accord with the view of the writers on pediatrics (Parrot, Baginsky, Henoch, Widerhofer, Comby, Soltmann).

SCLERŒDEMA; SCLEREMA ŒDEMATOSUM

Symptomatology.—The disease usually begins with vague prodromal signs, such as lessening of the appetite, slight restlessness and crying; and at the same time the breathing becomes shallow and irregular and the heart's action weaker. After a few hours the œdema is seen on the back of the feet, on the cheeks and also on the mons veneris. The œdema spreads upward, leaving the chest free, and is most extensive on the lower extremities. The hands and arms are also attacked but rarely the eyelids and the rest of the face. The penis and scrotum are in like manner swollen. The skin over the affected parts is tense and usually cyanotic in premature children; but in children born at term or when the affection occurs somewhat later, after the physiological exfoliation has terminated, the skin is pale, waxy and at times mottled.

An increase in volume is apparent; the consistency in less severe cases is that of butter (Heubner), but in advanced cases the skin is hard and stiff and distinctly gives the sensation of coldness to the palpating finger. The child lies still and apathetic, the temperature in mild cases,

* Scleroderma, the scleroderma of adults, which occasionally occurs in children and even in young nurslings (Cruse, Neuman, et al.) has nothing in common with sclerema or scleroderma of the newborn.

35–34° C. (95°–93.2° F.), sinks in severe cases to 32° C. (89.3° F.) and lower. The excretion of urine is scant and its amount is of some prognostic value. Albumin is usually not present. The body weight does not always diminish, as is usually stated, but on the contrary may even increase.

In the severer cases the children die with gradual weakening of respiration and the heart's action, and with increasing stupor. Death takes place usually after four to five days, in protracted cases after one to two weeks, although cases of lesser severity frequently end in recovery.

Actual complications are rare. Pneumonias occurring simultaneously, diseases of the navel, pemphigus and sepsis are to be considered as independent affections.

Fig. 18.

Sclerœdema in the newborn. Thinning of the epidermis and flattening of the papillæ, extensive softening and thickening of the corium with widening of the lymph-spaces and lymphatic vessels.

Occurrence.—Sclerœdema occurs only in the newborn. Seldom congenital, it begins, as a rule, on the second to fourth day of life, rarely later, up to the second week. Premature and debilitated children, twins and hereditary syphilitics are especially affected. It is also rather often observed with congenital heart disease and nephritis. Less severe forms are very frequently encountered in premature children.

In winter and in localities where the climate is cold, many more cases come under observation. The disease is encountered more frequently in hospitals and dispensaries, that is, it is more common among the poorer class of people than in private practice.

Pathogenesis, Nature.—This disease, concerning the etiology of which much uncertainty exists, is dependent, for its origin, on several factors.

The peculiar anatomical relations in the newborn, and especially in the premature or debilitated newborn, furnish a suitable basis for its occurrence.

On the one hand muscular and circulatory weakness, on the other a lowering of the oxidation processes and of respiration, are involved in the causation of sclerœdema. The influence of cold on the infantile organism becomes the exciting factor.

The nervous theory (Liberali, Ballantyne, G. Somma) and also the

theory of an infectious origin, are more hypothetical and have received no general recognition. Luithlen unqualifiedly denies the existence of sclerœdema as an entity; he classes it with the other œdemas of the newborn, with which it shares a common etiological basis, differing only by the superaddition of the elements of cold.

Pathological Anatomy.—Except for an occasional degeneration of the heart muscle (Demme) the usual findings are a venous congestion, especially in the distribution of the vena cava; and then congestion of the lungs, atelectatic areas and small hæmorrhages in the lungs and pleuræ. The œdema itself is not necessarily confined to the skin and the subcutaneous tissues but may on the contrary spread to the deeper lying muscles.

Reference is made to the illustration for the histological findings.

The **diagnosis** is easily made in pronounced cases. The pitting of the skin, on pressure with the examining finger, serves to differentiate the rarely-occurring sclerema, which feels much harder and with which the penis and scrotum are uninvolved.

Acute erysipelas is differentiated by its color, localization and the fever usually accompanying it.

The **prognosis** is favorable in mild cases, but becomes more dubious the more extensive the involvement; and also when other complications (atelectasis, pneumonia, heart disease) are present.

Prophylaxis.—This consists in the prevention of any immoderate chilling, especially with premature and debilitated children, and the instituting of breast-feeding.

Treatment.—The treatment consists primarily in the furnishing of artificial heat (couveuse). (See chapter on prematurity and debility.)

The stimulation of respiration by means of oxygen inhalation, combined with artificial respiration, is recommended. Hot baths, 38–42° C. (100.2–107.3° F.), with massage and passive motion in the bath or after it (Soltmann); inunctions with glycerine to which 10 per cent. of iodide of ammonium has been added are recommended by Badaloni; diuretics and digalen $\frac{1}{2}$–1–2 drops internally. Hot sweetened coffee (50–100 Gm.), possibly per rectum.

Where there is difficulty in swallowing, gavage and nutrient enemata. Breast-feeding must be employed if possible.

SCLEREMA

Clinical Description.—The onset of sclerema is similar to that of sclerœdema in that it affects the lower extremities, especially the calves, in a symmetrical arrangement. On careful palpation even in the early stages of the disease, a doughy sensation can be felt in the deeper layers of the skin. This soon extends over the thighs, trunk, and neck. The head and upper extremities are the last to be involved. The penis,

scrotum, soles of the feet and palms of the hands remain free. The induration increases so that the skin gives a sensation of board-like resistance and coldness. Various descriptions of the color of the skin are given by different authors. Neumann describes it as yellowish white and waxen; Heubner as grayish brown; and Parrot as light blue and cyanotic. Small ecchymoses may occasionally be found on the lower extremities.

The skin is immovable and hard and cannot be raised from the underlying tissue. In contradistinction to sclerœdema the affected parts become atrophied. The legs are rigid and the children are motionless like a stick of wood. The face has a mask-like appearance.

Fig. 19.

Sclerema of the cutis in the newborn. Extensive thinning of the epidermis with flattening of the papillæ. Diffuse sclerosis of the superficial layer of the corium and hyaline degeneration of the connective tissue. Partial round-celled infiltration of the vessels of the corium.

The general condition is bad, the weight falls rapidly and the temperature is constantly subnormal and may reach 30° C. (86° F.) or lower. Nursing and feeding are difficult on account of the rigidity. The mucous membranes are extremely dry. The respiration is lowered to 16 or even less a minute and the pulse falls to 50 or 30. Older children will give a shrill cry (cri de détresse) at frequent intervals. Convulsions may occur. The sleep is generally disturbed. The amount of urine is diminished and has a heavy sediment. Albumin is absent. The bowels often do not move spontaneously. The child generally dies in a coma after a few days. The course is the more rapid and fatal the younger the infant. The author has had cases of infantile atrophy in which this disease ran a prolonged course lasting weeks and ending in recovery.

Occurrence.—Sclerema, in contrast to sclerœdema, is a very rare affection. It occurs not only during the first days of life but also up to the first three months (Berthod) in debilitated, premature and poorly nourished infants. Knöpfelmacher puts the age-limit for its occurrence at the sixth month. It is observed more often in summer, since it occurs, especially in older nurslings, as a sequelum of cholera infantum and chronic catarrhal enteritis in the stage of atrophy (Parrot, Henoch). Congenital cases do occur, however, although with extreme rarity.

Nature and Pathogenesis.—According to Luithlen one must differentiate two forms of sclerema; one apparently autochthonous, that is occurring independent of any other disease; likewise a second form developing as the result of profuse losses of plasma or as a consequence of effusions into body-cavities (pleuritis, internal bleedings). This author assigns more of a symptomatic rôle to sclerema.

Essentially the process consists in a drying up of the body (Clementowsky, Widerhofer, Soltmann). The peculiar composition of the fat in the newborn and young nursling according to the investigations of Langer and Knöpfelmacher seems to furnish the basis for the occurrence of sclerema. The fat of a newborn contains only 43.3 per cent. of oleic acid (Knöpfelmacher) against 65.0 per cent. in the adult and in older children (Langer); whereas the amount of palmitic and stearic acid is greater (31:10) in the young nursling and congelation takes place at a higher temperature than in older children.

Later researches (Thiemich and Siegert) have left these findings again in doubt.

The lowering of the external temperature must play an etiological part also in sclerema, however not directly through the effect of the cold but indirectly by unfavorably affecting the respiration and circulation. Cases occurring without previous fluid losses and without the influence of cold are rare and etiologically totally obscure. A few authors (Schmidt, Aufrecht) have assumed an infectious origin for sclerema although the adduced bacterial findings only go to show that sclerema can occur after or with septic disease in the newborn.

The hypothesis of a vasomotor and trophic vagus-neurosis (Mumesci d'Agata) has found very few supporters.

Pathological Anatomy.—The anatomical findings are commonly negative. The usual findings are only those of atelectasis in the newborn, or else the evidences of a more or less acute enteritis in older nurslings. The extreme dryness is striking as well as the hardness of the tissues, on section of the skin and underlying connective tissue. The adipose tissue is firm, dry, stearin-like and resembles a piece of raw congested fat (Luithlen); concerning the histological features reference is made to the illustration (Fig. 19).

The **diagnosis** is made from the board-like stiffness of the skin together with the markedly abnormal temperature of the body. The decrease in volume of the members, the lack of the shiny appearance of the skin as well as the failure to pit serve to differentiate this condition from sclerœdema (also see section on scleroderma). Scleroderma, which usually comes in older and stronger children, differs from sclerœdema in its sharp demarcation and limitation to island-like patches and also in its favorable course (Cruse, H. Neumann).

The **prognosis** is generally bad in the newborn, but somewhat better in older children.

The **prophylaxis** consists, as with sclerœdema, in the avoidance of sudden and violent chilling, especially with debilitated and premature nurslings.

The **treatment** resembles that of sclerœdema (q.v.) in many respects. The most important and beneficial measure is a subcutaneous injection of salt solution [50–100 Gm. (℥iss–℥iii) of a 3d 1000 sodium chloride solution]. This can be injected two or three times daily or 10 Gm. (℥iiss) normal salt solution [sodium chloride 4 Gm. (℥i) sodium bicarb. 3 Gm. (gr. xlv) water to 1000 Gm. (1 quart)] three times a day, thoroughly sterilized and given at a temperature of 40°–42° C. (104°–107.5° F.). High rectal injections of normal salt solution can be used in conjunction with the subcutaneous method.

DISEASES OF PUBERTY

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AT the end of childhood, even before growth is fully attained the human being is capable of reproduction. This period of development is known as puberty.

The chief expression of beginning sexual power is the developing specific activity of the embryonic glands. Spermatozoa mature in the testicles of a boy, ova in the ovaries of a girl. In the case of the latter, the fully developed ova are discharged regularly, about every 4 weeks with the evidences of menstruation. Nocturnal, involuntary discharges of semen begin in boys, generally before they are completely developed sexually; these take place at first at long intervals.

Physiology.—Besides these events which constitute the nucleus of the development, many changes are to be observed in body and mind, the sum total of which we call the symptoms of puberty. Striking changes take place in the sexual organs; the external and internal genitalia become more vascular and grow rapidly; axillary and pubic hair appear, "Pubertas a pube dicitur"; in boys the beard begins to grow and hair appears on the rest of the body, especially on the chest and back. The figure, which up to this time has been childish, changes in a typical way, the shoulders become broader because the thorax increases greatly in breadth; its circumference grows in 3 years about 12 cm.; the maximum capacity of the lungs often increases 500 c.c. in a year. The breathing in females becomes more and more costal in type, in males abdominal, whereas before this the character often varied. In addition to the great general bodily growth which attends the development of puberty the sexual type becomes more apparent. The breasts of girls protrude and increase in consequence of the development of fat and connective tissue, moreover the branching of glandular ducts proceeds, though glandular tissue capable of function develops only in the periphery of the breasts. The female pelvis widens in all dimensions and the thighs and buttocks become rounder and fuller in consequence of a marked deposit of fat. The plastic development of the extremities in youth is caused by a growth of the skeleton but also by an increase in the size and firmness of the muscles.

Of the changes in the inner organs that of the larynx, which brings

about the change of voice, is first to be mentioned. This is in general more marked in boys, in whom the larynx grows rapidly, especially in the transverse diameter with corresponding increase in length of the vocal cords; the female larynx on the other hand, grows more in the vertical diameter. Girls' voices break less often than boys and generally only in singing, though they become more resonant and fuller. Boys' voices are rough and harsh and after a time of frequent breaking become finally an octave lower. The connection between change of voice and sexual development is evidenced by the well-known fact that boys, castrated before puberty, show a decidedly smaller growth of the larynx and retain very high voices. The dependence of the development of the sexual character upon the growth of the embryonic glands can be well seen in these individuals; males castrated before puberty show in addition a diminished growth of beard, slender figures, narrow chests and broad pelves.

The connection between the thyroid gland and puberty and growth rests upon numerous observations. The thyroid gland, in which a congestive and parenchymatous swelling occurs before and during puberty causing an increase in the organ of 15 per cent. and at the time of menstruation frequently 60 per cent. (Fischer, Freund), has also a decided influence upon bony growth. Thyreoidin can be used satisfactorily to influence a cessation of this, so long as the cartilages are not calcified (Denis, J. J. Schmidt). Dysthyreoidia has not only a restraining influence upon physical, but also upon mental development and further, the special morphological growth of the genital organs of both sexes and the development of puberty are dependent upon the normal growth and function of the thyroid gland (Hertoghe). The connection between the thyroid gland and the sexual organs is shown also by pathological facts such as the diminution of sexual power in men and anomalies of menstruation and atrophy of the sexual organs in many women during the course of Basedow's disease, the development of which not infrequently dates back to the age of puberty (Grawitz). If, as Hofmeister says, the thymus gland can take the place of the thyroid gland after experimental extirpation of the latter, the physiological importance of the thymus disappears with its beginning involution which takes place often long before the child enters upon puberty.

Among the processes of growth that take place at puberty that of the heart is very marked. In the previous years this has remained relatively small, increasing 6 per cent. to 7 per cent. each year, but at puberty it grows rapidly and shows an increase as great as 20 per cent. The considerable growth of the lungs is evident from the figures that have been mentioned in regard to the circumference and capacity of the chest. The growth of the liver and kidneys is also worthy of mention. The brain continues to grow even into the third decade.

The above-mentioned changes in the sexual organs that serve to indicate puberty, take place inside a period of one to two years. The general bodily development as regards growth and increase in weight occupies a longer time. Upon these relations, important for an estimation of the physiology, pathology and hygiene of later childhood, we possess a great number of facts which have been obtained through the systematic measurements of some 100,000 school children in the different countries of Europe and America. According to Axel Key the average growth could thus be decided with certainty. From this valuable material the following facts are here quoted: the increase and growth in weight and length exhibit periodic changes and do not follow each other closely; growth in height is very apt to precede increase in weight. In later childhood, before puberty, a period of slow growth and increase in weight occurs; then from the tenth year on girls begin to grow more rapidly and this growth lasts about five years with its maximum in the twelfth year. An increased gain in weight which characterizes the more vigorous time of puberty lasts from the twelfth to the fifteenth year. While growth generally stops at the seventeenth year, marked increase in weight continues as late as the twentieth year. In the case of boys a decided growth lasting four years begins in the fourteenth year and the maximum of this is in the fifteenth year. The weight increases mostly in the sixteenth year. The sixteenth and seventeenth years are the years of greatest development for boys. Boys until the eleventh year exceed girls in length and weight, the latter are larger until the sixteenth year and from that time on drop behind the male sex.

The strength of build is generally dependent upon the development of the chest, whose circumference stands in nearer relation to the weight than to the length. Children who have grown up in poor surroundings remain in weight and length constantly behind those of their own age in better circumstances. The period of slow development noticeable in all children before puberty is lengthened in the poor, in these puberty begins later but this stage lasts a shorter time and is ended in the same year as in children of the classes better situated.

Besides the above-mentioned effects of age and of outward circumstances upon the bodily development of the child, the influence of the time of year can in general also be noticed, in so far as during the winter months a slight increase takes place, in spring and summer a growth in height, often with loss in weight, and finally in the fall decided increase in weight results. Likewise changes in the outward temperature are operative, in so far as an increase in temperature at any time of year, even though it lasts only a few days, causes an increase of growth and a fall in temperature causes a diminution of growth.

In general, puberty begins in girls of all peoples and climates earlier than in boys. The beginning of the formation of semen takes place in

the latter, in the majority of cases, not until the fifteenth year, while complete maturity is generally considered to be reached at eighteen years. The age at which boys become sexually mature and girls menstruate for the first time varies under the influence of climate, hereditary predisposition, race, social position, method of life, and individual peculiarity. The higher the mean temperature of the native climate the earlier puberty appears. Menstruation begins in Germany most commonly in the fourteenth or fifteenth year with less frequency before the thirteenth or after the eighteenth year. It is earlier in girls living in cities and in better circumstances than in those living in the country and in poorer circumstances. The previous use of alcohol can through the excitation of sexual desire, cause an abnormally early beginning of menstruation and premature sexual intercourse has the same effect. Girls of sanguine temperament, of nervous irritability, of large stature and of strong constitution menstruate earlier than phlegmatic individuals or than small or weak girls.

The arrival at maturity shows itself in children by various manifestations that are noticeable in part subjectively and in part objectively and of these some can periodically recur. First of all cardiac palpitation is commonly noticed, and besides this, vertigo, a sense of oppression, shortness of breath, nose bleed and headache are not infrequently seen. (This will be more particularly dealt with under the relation of puberty to the circulation.) Especially in girls one sees premonitorily as an expression of a congestion toward the genital organs an occasional sense of pressure, weight and twinges in the lower abdomen, tenderness in the region of the ovaries and spasmodic pain in the abdomen and lumbar regions, the former radiating toward the epigastrium and the latter toward the thighs. Transient and even painful pricking or tension in the breasts and twinging pains along the ribs are common symptoms present oftener in girls than boys. Besides the bodily transformations that indicate puberty, mental changes make their appearance. New sensations develop. Boys learn from emissions the specific sexual sensations out of which an impulse to attain such a sensation can develop. The awakening of the sexual impulse is dependent, irrespective of the progress of bodily development, upon the exciting influences of environment (persuasion), education (sensual excitation from bad literature, immoral pictures), and food (too nourishing food, the use of alcohol). We will speak in the chapter on masturbation of the effect of an abnormal, hereditary predisposition and of the irritation of the genital nerves by phimosis and other local bodily anomalies on the one hand and of early provocation of the sexual sensation on the other. Under normal circumstances the sexual impulse of boys first shows itself only in occasional erections and likewise in a friendly affection for girls, provided that the company of girls is not at first despised. Emis-

sions and such acts do not take place in normal girls and to them at first sexual sensations are still foreign (Löwenfeld); on the other hand specific female characteristics show themselves, such as solicitude for younger brothers and sisters and tenderness for strange children. In addition young girls, as is well known, readily idealize a teacher, an officer, favorite actors, etc. In general the mental changes in maturing girls take place more quietly than in boys in whom the growing sense of manhood often finds expression in an increased sense of importance and an arrogant disposition (Emminghaus). In consequence of this change of disposition we notice more often in boys than in girls a peculiar transformation of the mental and bodily power that characterizes these years. This shows itself in chaffing and teasing of those younger and weaker, derision of the infirm, cruelty to animals and foolish acts of all kinds. Also against parents and teachers a sense of superiority is felt; their warnings are laughed at and the reaction against them amounts to insubordination and even rising animosity. Falsehood and bragging, sentimentality and extravagance are evidences of the frequent mental variations. Depression and buoyancy abruptly alternate. This unsteadiness of mind is evidenced by the often clumsy, awkward and clownish movements of the rapidly growing body. The rapidity of the mental growth is subject to great variations, sometimes the intelligence develops more rapidly, at other times the emotions alone. Bodily and mental progress do not take place throughout in parallel lines, it is more common for the mental development to stand still when bodily growth is accelerated. The psychical changes mentioned above continue beyond the time of bodily development and only in the eighteenth year or later is the boy relieved of this disturbing experience. It must be confessed, however, that from this time permament psychical disturbances may date.

Pathology.—Puberty may be premature or delayed. Under the head of premature development we see an early mental and bodily development going hand in hand or independently following one another. The early bodily development usually consists in a more rapid growth of the body without corresponding involvement of the sexual organs but less frequently sexual maturity is independent of and precedes bodily development (Kussmaul). There are numerous observations of menstruatio præcox (before the tenth year) upon record even in children during the first year, in whom in addition to a disproportionate development of the breasts and outer genitalia regular bleeding took place usually at considerable intervals. Menstruation in these cases is however rare. Pregnancies progressing in a relatively normal manner have also been recorded as early as the eighth or ninth year. This early menstruation is referred to congenital errors in development with premature bodily growth as its result, to excessive maternal pro-

ductiveness, to diseased conditions in the ova, to irritation of the trophic centres (hydrocephalus, shock) and to sexual excitation. In those who mature early, bodily growth generally ends with complete sexual maturity. Early maturity is sometimes combined with enormous fat formation which latter can appear early by itself or can accompany a precocious bodily growth without early sexual power. Girls may show a sexual prematurity alone; but in boys this early sexual development generally goes hand in hand with an early development of the whole body. Emissions of semen have been noticed in such boys very early, from the second year on. The mental growth does not progress parallel with the bodily development in those early matured, it seldom precedes it, usually it takes place later.

Amenorrhœa can be simulated by atresia of the uterovaginal canal; in consequence of the collection of blood behind the atresia with distention of the vagina, uterus and tubes, hæmatocolpus, hæmatometra or hæmatosalpinx may arise (Gebhardt). In consequence of congenital heart disease (pulmonary stenosis) there may be a deficient development of the genitalia. With congenital aplasia of the ovaries, the uterus is also insufficiently developed and ovulation and menstruation are absent. Menstruation can hardly take place if functionating ovaries are combined with a rudimentary uterus but it may evidence itself in the form of pains and nervous disturbances recurring periodically and with intensity. A fœtal uterus can be suspected if the breasts do not develop or if the pubic hair fails to appear at the proper time. Errors in the development of the inner genitalia in girls are first clinically noticeable at the time of puberty, but even before this deficient development of the ova causes a retardation of bodily growth. Functional amenorrhœa in the years of development is not infrequently noticed after a sudden change of social or climatic conditions and further, in consequence of constitutional anomalies such a chlorosis, anæmias of all kinds, after acute infectious diseases, in tuberculosis, severe syphilis, nephritis, neuroses, psychoses, diabetes, leukæmia, Basedow's disease, alcoholism and morphinism. When menstrual bleeding fails or is deficient in quantity even at the age of puberty the appearance of periodically recurring, vicarious bleeding, from the nose, gums, lungs, stomach, hemorrhoids, nipples and ears is sometimes seen.

Independent of the local premonitory disturbances that have been previously mentioned (p. 114) we sometimes find even at the first menstruation prodromal, concomitant or succeeding cramp-like abdominal pains (especially in the case of nervous or chlorotic girls or with hypoplasia of the uterus). In connection with the nervous system, vertigo or intense headache may be noticed; functional stomach and intestinal disturbances (such as regurgitation, vomiting, cardialgia, diarrhœa, constipation or flatulence) can appear. The congestive sacral pains are

sometimes accompanied by a desire for urination or defecation. At the age of puberty reflex angioneuroses are also found. Besides the premenstrual sensations of heat and cold, erythemata, urticaria, eruptions of herpes are noticed prodromally or concomitantly and further as a forerunner periodic painful œdema of the extremities may be found.

The revolution which at the time of puberty attacks especially the sexual organs, often affects the male breasts. The atrophy of these generally takes place at this time without symptoms. Nevertheless, a sensitive swelling of one or both breasts may sometimes occur with reddening and pigmentation of the nipple accompanied by first dull and later sharper pain. These sensations are often referred to trauma and disappear spontaneously in the course of a few weeks. They may however recur, but the breasts rarely remain enlarged (gynæcomastia) in which case a deficient growth of the genitals would also be noticed. In both sexes at puberty a circumscribed nodular swelling of the breasts can be caused by a growth of interstitial connective tissue but this also disappears later on and seldom is it the point of origin of a new growth.

In the male genitals unpleasant sensations sometimes occur because of an incomplete descensus testiculi which up to that time had not been observed. With retentio testis inguinalis (less commonly with the abdominal or perineal variety) boys complain sometimes of drawing pains in the testicle (or spermatic cord). Sharper pains during puberty are caused especially by inflammatory irritation which occurs readily after injuries (gymnastic) or after mumps, etc., in consequence of the confined position of the retained testicle. As retained testicles not infrequently become atrophic and further show a tendency to malignant degeneration, removal of the testicles is to be considered provided a hernia pad especially constructed and to be worn without intermission does not hold the testicle constantly pressed below it (Heidenhein). Analogous to the displaced testicles of boys changes in position of the ovaries (ovarian hernias) are apparent in girls especially at puberty, through periodic swelling of this organ (Hennig). At puberty not infrequently cases of pseudohermaphroditism can be determined as to sex, as retained testicles pass into the sides of the scrotum separated by an extreme hypospadias and in addition changes follow in the characteristics of the child which up to that time seemed to be feminine. Phimosis also can give rise at puberty to manifold disturbances. At this time especially, a quantity of readily decomposing smegma is produced whose retention leads to balanitis and balanoposthitis with a foul smelling discharge which can simulate gonorrhœa. A microscopical examination of the secretion for gonococci prevents error. Successful treatment is only possible after operative removal of the phimosis; this is further to be considered when with a narrow prepuce enuresis or masturbation comes on at puberty.

The chief development of a systematic practice of *onanism* occurs (according to Fürbringer) at puberty. Provided that this bad habit has not already been practiced, a local irritation of the genital nerves (through eczema, prurigo, phimosis or vulvitis with an accumulation of smegma, oxyurides, stone in the bladder, constipation) plays the part of an exciting cause in connection with the awakening sexual passion (see page 114). This complaint is more often the outcome of a neuropathic disposition with hereditary weakness of will than the result of an excessive hereditary sexual desire (Löwenfeld). Idiots, those mentally deficient, and epileptics often show a decided tendency to onanism. In boarding schools (occasionally breaking out epidemically in consequence of living with certain depraved scholars) the evil is commoner in boys than in girls. Provided there is no excessive practice of this evil habit, striking symptoms on the side of the nervous system are not to be found in otherwise healthy individuals. But one sees in habitual masturbators in addition to anæmia and an exhausted appearance not infrequently the signs of general nervousness with migraine, sense of pressure in the head or of cardiac neuroses, with palpitation and sense of pressure or spinal symptoms (exhaustion, paræsthesia in the legs, sacral pains and other annoying sensations in the back). The association during the period of development of intense mental effort with excessive onanism injures the brain in its power of resistance and accomplishment; beside loss of energy, lack of memory, indisposition and incapacity to work, absent-mindedness is often a striking symptom. Sexual neurasthenia not infrequently begins at puberty. The evil results of masturbation can be completely overcome by early and rational opposition. Positive local signs in the genitalia, apart from slight evidences of irritation, are not to be determined. For the purpose of prophylaxis the above-mentioned bodily anomalies that lead to irritation of the genital organs are to be removed; of importance also is food causing as little irritation as possible (especially the avoidance of alcohol). Reading and companions should be overseen, often severe bodily exercise out of doors is of advantage and further the awakening of a mental interest sometimes by travelling. If the evil persists the moral influence of parents and teachers is often of value in addition to these other measures; there is less to be accomplished by severe punishment than there is by kindly explanation, if necessary with the assistance of the physician. If on the one hand as can be seen by the foregoing description, sexual development gives rise to most manifold disturbances, so on the other hand at puberty occasional functional disturbances occur in almost all the organs which may often have sweeping and enduring consequences, and the general health at this time is subject to great variations. A consideration of the ratio of disease during this age of development gives us the following striking facts. We gather from the

statements of Axel Key, Hansen, Hertel and others which claim the greatest possible accuracy, that in the middle grade schools the general sickness of boys reaches nearly 40 per cent. and of girls 60 per cent. and over. While by the latter anæmia amounts to 40 per cent., by the former myopia occupies the first place. Sixteen per cent. of boys suffer from chronic headache, 36 per cent. of girls, of the latter 10 per cent. have spinal curvature. Of chronic diseases it has been determined, that those of the lungs amount to $3\frac{1}{2}$ per cent., of the heart 3 per cent., and of the gastro-intestinal tract $2\frac{1}{2}$ per cent. From personal observations of 2500 cases observed in the last four years in the pediatric polyclinic and of 500 from private practice, 260 suffered from acute infectious diseases, 354 from tuberculosis, 7 from syphilis, 325 from anæmia and chlorosis, 350 from diseases of the respiratory organs, 580 from diseases of digestion, 90 from diseases of the urogenital organs, 280 from skin diseases and 60 from organic heart disease. Disturbances were found in 600 cases which could be brought into more or less close connection with puberty. Of these 22 per cent. had general evidences of menstruation, drawing and other kinds of pains in the breasts or abdomen without objective physical signs; 16 per cent. had cardiac neuroses, 16 per cent. goitre, 16 per cent. periodic headaches, 15 per cent. neurasthenia, 15 per cent. hysteria, 7 per cent. epilepsy, 4 per cent. chorea and 6 per cent. the albuminuria of puberty. Of the chronic infectious diseases, tuberculosis at this critical period is of the utmost significance on account of its great frequency and its often fatal result. According to Kirchner, between the ages of ten and fifteen, the deaths from tuberculosis in males increase from ten to sixteen in a hundred deaths and in females from eighteen to twenty-six in a hundred. After tuberculosis the anomalies of the blood—especially chlorosis—take the first place. As far as the diseases of the single organs are concerned those of the respiratory and digestive tract are not infrequent and affections of the skin still show a great frequency. Functional disturbances are found in 20 per cent. of children at puberty according to my observations and these are to be referred to the processes of development; three-fifths of these affect females and two-fifths affect males.

Let us now turn to the *diseases of the special organs* or systems in so far as they are made evident during puberty by special symptoms or by great frequency. In the increased general bodily growth which accompanies puberty the bony and muscular systems are chiefly involved and the diminished resistance (insufficient firmness of the skeleton and relative weakness of the muscles) which occurs in consequence of this gives rise to the most various disturbances. In the first place, curvatures of the spine—especially lateral curvatures—occur at this time in consequence of customary but improper attitudes at school and in housework; further, in consequence of unilateral muscular exercise

(for example violin playing and tennis) and in consequence of unilateral loading of the body (the carrying at the side of heavy school bags, etc.). Genu valgum can also develop at this age by reason of prolonged standing. The changes that have been mentioned are the more easily produced according as bodily exercise has been disregarded in consequence of an education devoted too exclusively to mental improvement and further when by reason of improper food at this critical time the composition of the blood becomes deficient or was deficient from the beginning. The possibility of late rickets has recently been emphasized from the surgical side (Roos, H. Curschmann) as a cause for genu valgum and also for curvatures of the spine or for flattening of the pelvis in so far as these anomalies develop during puberty. With the increased processes of ossification that go on at this time analogous to those at the infantile period of bony formation a special disposition to rachitic disease is supposed to exist. At this stage of rapid growth a slight amount of bodily fatigue easily occurs and forced exertion undertaken concurrently with stronger comrades, especially in sports, gives rise to overexhaustion. This shows itself generally in addition to a general weakness in a somewhat diminished motility of the joints and in pain on pressure over the epiphyses chiefly involved in growth without other objective changes. These are the upper epiphyses of the humerus and tibia and the lower epiphyses of the radius and femur. The pains which generally disappear rapidly are described as growing pains (especially in France by Poncet, Bouilly, Comby) and growing fever is also described. These are statements which we should accept with caution. Certain it is that at this time pain in the extremities results from slight trauma or overexertion and also with rheumatic and other febrile infections following which as is well known a more rapid growth often occurs (poussée de croissance).

Finally the multiple cartilaginous exostoses developing only on bones still in the process of growth and which occur from an inherited source, should be mentioned in this place. These generally appear as symmetrical, hard, painless indurations and rough tumors in the neighborhood of the epiphyses from which they may be separated in the process of growth.

Of the myopathic muscular atrophies the infantile muscular dystrophy with pseudohypertrophy (of the calves, thighs, gluteal and deltoid muscles) and the infantile muscular hypertrophy (without pseudohypertrophy) with involvement of the muscles of the face are likely to develop before puberty. During the period of puberty the so-called juvenile form of muscular atrophy appears with the initial involvement of the shoulder-girdle muscles and later the muscles of the upper arm (with the exception of the deltoid, supra- and infraspinatus and coracobrachialis) and finally the muscles of the back and pelvis.

Anomalies of the *blood* are a decidedly common phenomenon at the age of puberty. These, so far as the anæmias are concerned, date from some previous time or occur very easily in consequence of severe acute infectious diseases, protracted fevers following irrational methods of life (improper food, athletic exhaustion) or unhygienic living or working conditions. Tuberculosis, kidney affections, constipation and entozoa are always to be thought of. An absolute predisposition for chlorosis exists in the female sex, the blood of which is from the beginning poorer in red blood cells by nearly half a million per cmm. but besides this (according to Jones following Grawitz) it shows especially at puberty a relatively smaller hæmoglobin content. The number of leucocytes is higher at puberty, 9–12000 per cmm. (Bayer). For a further consideration of chlorosis see the chapter on blood diseases.

In the *circulatory system*, disturbances frequently arise at puberty in the form of cardiac palpitation, sensations of pressure, vertigo, syncope and shortness of breath. Only when alcohol, nicotine, kidney disease and overexertion can be excluded as causes, is a direct connection with puberty to be considered. Objectively one finds an enlargment of the right or left side of the heart (sometimes both sides) with a soft pulse and an apex beat which may be exaggerated without an evident increase in size of the heart and this generally with an accentuated second aortic sound and often with an accentuated second pulmonic sound. Sometimes the sounds are ringing in character. The tension is seldom increased and the arteries rarely tortuous. Systolic murmurs at the apex or in the second left intercostal space are heard with and without an accentuated second pulmonic sound. The pulse is increased in frequency and may sometimes be irregular. An excited heart action at the time when various organs show an increased excitability can be simply evidence of irritation (Krehl) but generally there is an actual disproportion between the development of the chest and the size of the heart, a decided increase in the cardiac volume and a relative narrowness of the blood vessels; a further disproportion can also occur between the rapid expansion of the blood vessels in consequence of a sudden growth in length (especially after afebrile diseases) and an undeveloped heart which cannot meet the increased demands made upon it. An insufficient growth of the heart generally goes hand in hand with a retarded growth of the whole body and especially of the sexual organs: hypoplasia of the heart is generally congenital as is also an especial narrowness of the large blood vessels, but this nevertheless frequently manifests itself only at puberty (Berg). The subjective and objective phenomena which have been mentioned begin without any apparent outward cause, continue for a long time with more or less regularity or may periodically increase, especially the subjective symptoms. A complete disappearance of the cardiac symptoms generally follows the completion of puberty,

by virtue of a readjustment of the equilibrium. Not so very infrequently an exaggerated apex beat remains permanent and this may also be true of a functional weakness which shows itself later on in frequent attacks of weakness, of syncope, etc., following slight exertion or excitement. The prognosis of the cardiac disturbances at puberty is to be made with caution, as transient changes in the size of the heart are not always to be distinguished from definite changes in the muscle. Prophylactically and therapeutically, caution is to be exercised against the influences which can injure the heart, such as excessive meat eating, alcohol, nicotine, coffee, tea, sexual excitement and especially against athletic overexertion. When on account of the increased growth of the body, the heart must accomodate itself to increased demands, a nutritious non-irritating diet is necessary as well as sufficient bodily rest and exercise corresponding to the patient's present condition. This can best be accomplished by moderate out-of-door exercise, walking, etc. Children with valvular disease not infrequently show at puberty extreme cardiac disturbances on account of the association of functional disorders with the valvular lesions.

The *thyroid gland* whose connection with puberty has already been mentioned (p. 112) shows not infrequently a strumous degeneration in addition to the temporary or periodic conjestive tumefaction which has been noted. This is sometimes noticed in earliest childhood on the basis of an inherited predisposition but is most commonly observed in the fourteenth or fifteenth year or in the two following years. It is more frequent in females in whom this gland is from the beginning more developed (Demme). While the physiological congestion is transitory in puberty, mechanical causes at this time can give rise to a chronic congestion; these may be, carrying heavy weights on the head and neck, excessive singing exercises, tight bands around the neck; the congestion may also be influenced by pertussis, chronic pneumonia and valvular lesions. For the different forms of goitre see the article by Siegert in Vol. III.

There are no affections of the *respiratory system* that stand in close connection with puberty. The expectation that has been cherished by some that adenoid vegetations of the nasopharynx will disappear at this time or cause no more symptoms, on account of the increase of the pharynx progressing parallel with the increased bodily growth, is not fulfilled. Operative removal of the growths should be strongly advised in order that their continuance may not interfere with the permanent expansion of the chest.

With the change of voice that has been described on page 111, it frequently happens, more commonly in boys, that the voice is incorrectly developed. It may remain high or crowing, it often fails or cracks. In consequence of the rapidly following changes in the larynx in form and size, the proper sensation for the changing conditions of tension is

lost (Bresgen). Relative quiet for the voice (abstinence from singing or shouting) is prophylactically of value, for therapeutic purposes, practicing in a moderately loud voice with the deepest tones and possibly with slight compression of the larynx, is effective. In children who previously have had a tendency to diffuse bronchitis possibly with dyspnœa, one may see typical attacks of asthma occur if at the same time with the rapid increase in length that accompanies puberty, a delayed development of the thorax is present. These attacks of asthma can disappear entirely when growth is completed (Müller).

In so far as the *digestive system* is concerned, frequently recurring attacks of tonsillitis play a considerable part in the morbidity at this time; these attacks occur generally in individuals already predisposed to them. Various dyspeptic complaints are also seen which are characterized by their periodic recurrence, and in the absence of an irrational diet as a cause they are to be considered as nervous symptoms. Not infrequently gastroptosis and enteroptosis begins in these years, especially in females, influenced by constricting clothes, in connection with an irrational and excessive amount of food (Meinert). Ulcer of the stomach, which is almost never found in childhood, occasionally occurs at puberty. Functional motor disturbances of the intestine are decidedly common at this time; especially in girls chronic constipation is noticed and with this one has to contend not only with insufficient exercise and unsuitable food but often with a false sense of modesty. The abnormally long retention of feces or urine which not infrequently takes place in school girls can cause an ante- or retroflexion of the uterus (Hennig). Occasionally periodic attacks of diarrhœa are observed that cannot be explained by errors in diet; less commonly a sudden desire for stool with incontinence occurs, of a temporary congestive or nervous origin. Before the beginning of this period Quincke saw, in an otherwise healthy girl, twelve to fourteen years of age, an ascites slowly develop which disappeared rapidly at the beginning of menstruation.

Diseases of the *urinary organs* are not common in puberty; still the majority of cases of cyclic or orthostatic albuminuria begin at this period so that one can speak of albuminuria of puberty. The patients are often pale, tall, and slim individuals easily tired, with swollen eye lids and a tendency to headache, vertigo and dyspeptic complaints. The disturbances of the heart which have been mentioned on page 121, are frequently present. But in otherwise healthy individuals at puberty one finds a periodic excretion of albumin, sometimes more, sometimes less, in diminishing quantity in the night urine. This occurs often with uneven growth and with a backward general development. The urine shows a high specific gravity; sediment is absent (or a few fatty epithelial cells and hyaline casts); chemically the demonstration of an albumin precipitable by acetic acid (euglobulin) is important, for this in the

chronic nephritis of children is absent or only present in traces (Langstein). From the standpoint of differential diagnosis one must always consider the exclusion of such nephritides which can begin relatively without symptoms especially in conjunction with infectious diseases and may persist insidiously. The albuminuria of puberty disappears when the organism of the affected individual recovers its balance in consequence of better formation of blood and better nourishment with the completion of growth (in individuals with a congenital abnormal perviousness of the kidneys, the disposition to an excretion of albumin can remain permanent). Therapeutically a rest cure is not always successful; in place of this properly graded, systematic exercise with a view to greater general and especially cardiac development should be employed. Very exhausting bodily exertion should be rigidly excluded and long periods of rest observed. The food should be nourishing and sometimes the limitation of an excessive meat diet to a moderate amount is of value. In any event alcohol, coffee and spices are forbidden. Movable kidneys are found in girls even at puberty possibly from wearing constricting clothes (Rosenthal, Hollederer). The majority of cases of Addison's disease observed in childhood occur at puberty corresponding to the common appearance of tuberculosis at this age (Monti). Ogston found in a twelve and in a sixteen year old girl, besides hypoplasia of the internal genitals, greatly enlarged suprarenal glands. As far as the bladder is concerned persistent enuresis generally ends at puberty with a not infrequent increase in girls up to the beginning of menstruation. In boys this annoyance lasts more commonly into puberty when the prostate gland, which only develops to a considerable extent between the tenth and fourteenth years, gradually provides sufficient obstruction during sleep (Dittel, Bokai).

Acute infectious diseases come with the greatest frequency in earlier childhood; according to our observations scarlet fever and rheumatism are still striking at the beginning of puberty on account of the relatively higher morbidity. Mumps is noteworthy on account of the inflammatory metastases of the sexual glands (testicles, ovaries) which not infrequently occur, with severe local symptoms. As regards the chronic infectious diseases, the great frequency of tuberculosis at the period of puberty (page 119) has already been considered. Syphilis is infrequently observed either as a fresh infection following premature sexual intercourse or criminal abuse, or as late hereditary syphilis with which the symptoms of the inherited dyscrasia are not always observable in earlier childhood. Of the manifold evidences of this are here to be mentioned: hyperplastic periostitis of the tibia or of the head, sternum, etc., gummatous processes and further, obstinate chronic symmetrical joint affections (suggesting deforming arthritis), destructive processes of the nasal cartilage, of the soft parts of the lung and of the

pharynx with consequent star-shaped cicatrices, indolent glandular infiltration, Hutchinson's triad, from the side of the nervous system in addition to contractions and paralyses, lesions of the cranial nerves, also chronic enlargement of the liver and spleen generally without icterus or marked ascites and finally a retardation of the general and especially of the sexual development (Heubner, Hochsinger).

Of *skin affections* those that stand in close connection with an increased activity of the sebaceous glands, comedones, acne and furuncles are to be mentioned as common occurrences in the years of puberty.

Affections of the eyes with the exception of the great frequency of myopia at the time of rapid growth, are not infrequent and are to be considered in connection with the hyperæmia of the retina, optic nerve and brain. Acne of the edge of the lids (hordeolum) is often seen in those at puberty. To be mentioned are the pre-menstrual retinal hyperæmias with obscured vision and headache, disturbances in the chorioid membrane and retina, which consist of exudation and hæmorrhage, but these generally go on to complete recovery. Further to be mentioned are œdema of the head of the optic nerve with immediate improvement after the beginning of menstruation and a periodic return before each menstruation, atrophy of the optic nerve with amenorrhœa and fulminating transitory pre-menstrual amaurosis (Klopstock). In nervous individuals concentric contraction of the field of vision, asthenopia, hemeralopia and flittering scotomata are seen; sometimes there are hæmorrhages into the vitreous humour which recur until menstruation is regularly established. Anæmic girls may have a slight inflammation of the whole uveal tract (Gutman).

As has been mentioned above (see page 115) the nervous and mental life is concerned in a striking manner with the processes characterizing puberty. Children who have been previously healthy so far as their nervous system is concerned not infrequently exhibit phenomena at this time which at another time would be considered pathological. A congenital neuropathic disposition may now first become noticeable or irrational hygienic and pedagogic measures at home and in school may give rise to considerable nervous disturbances. First and foremost, *headaches* are a common occurrence with different localizations, sometimes recurring periodically, sometimes permanent, so that the ability to pay attention and to perform mental work may be very greatly affected. Active hyperæmia of the brain is not infrequently the cause of this; this phenomenon is often associated with vertigo, spots before the eyes and ringing in the ears and possibly also hyperæmia of the face. Passive hyperæmia often results from wearing clothes which compress the neck and body, from bending over sharply at work and from interference with nasal breathing. Overstraining of the eyes on account of anomalies of refraction is to be considered. Anæmia of the brain with

anomalies of the blood and insufficient nourishment can give rise to headache which also can be caused by mental overstrain. Other factors to be mentioned and which are also to be observed from a prophylactic standpoint are bad, and overheated air and deficient light while at work; further, dyspepsia and constipation and finally also alcohol and nicotine. The prophylaxis and treatment will be found under the general hygienic and dietetic measures for puberty on page 128. Hemicrania not infrequently appears at this time if it has not previously existed, in which case it may cease. Premonitory symptoms not infrequently precede the typical attacks of headache in the form of weakness, vertigo, depression and irritability; vomiting generally follows at the height of the attack and at the end quiet sleep comes on. Overfilling the stomach often acts as a cause as does the ingestion of alcohol, emotions and physical strain. We not infrequently observe at puberty the symptoms of general nervousness based upon an inherited tendency and this shows itself in the form of a permanent excitability with extraordinary sensitiveness to mental impressions and with explosive reactions; on the other hand we frequently meet the ready exhaustion characteristic of neurasthenia, caused by slight or moderate mental or bodily activity in which sensations of pressure in the head, languor, pain in the back and sleeplessness may appear. Especially in the years of puberty, *epilepsy*, which up to this time not infrequently has evidenced itself by the phenomena of temporary loss of consciousness, or in attacks of vertigo, reaches full development. The expectation often raised by the laity, that epileptic convulsions already developed may disappear at the beginning of puberty, is unfortunately seldom fulfilled; rather more commonly there is an aggravation of them. While the greatest frequency of *chorea*, especially the so-called rheumatic chorea, occurs in the school years before the time of puberty, chorea, especially in girls, can have its beginning at this time. In addition to the characteristic involuntary movements a psychical alteration is often very striking, in the form of irritability, absent-mindedness, weakness of memory and slight mental exhaustion. As causal factors, emotions (fright and anxiety) come into consideration. The chorea which on the basis of imitation breaks out occasionally in schools almost epidemically, belongs in the domain of hysteria. The congenital diseased tendency underlying this expresses itself in early childhood generally in single local symptoms of bodily functional disturbance such as hypo- or hyperkinesia. Accidents, emotions and psychical contagion are effective causes. With progressive bodily development a childish hysteria may disappear or show the characteristic protean and contradictory form of disease in which purely psychical conditions may with extraordinary rapidity take on the most various physical symptoms of disproportionate dimensions and duration. In addition to the typical convulsions, attacks

may appear simulating unconsciousness, later stupor, prolonged sleep and somnambulism, but this condition never goes on to dementia.

The appearance of conspicuous *mental weakness* is an early symptom of hebephrenia; this stands in close connection with the rapid and total change of the bodily and mental development and always appears in connection with puberty (Hecker, Kahlbaum). Generally the patients are individuals already backward in their bodily and mental development in consequence of previous illness, in whom, often apparently after an emotional shock, mental depression is first noticed (with delusions and impression of persecution); then excitement alternates with causeless mirth and a tendency to foolish speaking, in speech and in writing a delight in arbitrary imagery appears, often with a striking tendency to take up a subject over and over again; a sentimental method of expression, a forced tone full of meaningless phrases and affected speech are typical phenomena. An exaggerated impulse to be doing something is made evident by aimless actions, such as littering things about. These patients may remain for a long time at the mid-point of mental decay and during this time periods of excitement amounting to delirium may come on in consequence of outward causes such as menstruation or hallucinations. Generally the termination in a state of extreme mental weakness follows in the course of a few months often with destruction of the mind. If on the one hand the phenomena of hebephrenia in the initial stages are often merely the same that we meet in healthy individuals as transitory appearances at puberty, on the other hand, nevertheless, victims of dementia præcox often show certain peculiarities much earlier; these are a reticent, sly manner, whimsicalness, unruliness, irritability and moral instability.

In addition to the hebephrenic form of *dementia præcox* described above, other forms may begin at puberty and lead to marked mental weakness; the *catatonic* form for instance, in which, after an initial stage of depression, states of stupor alternate with excitement, and there appear characteristic phenomena of motor spasm and motor retardation; then the form similating paranoia, characterized by hallucinations and illusions as well as by rapid mental decay. Other psychoses may now and then be observed at the time of puberty, and it may be worthy of note that *paralytic dementia* not infrequently has its beginning at this period, attacking both sexes with about equal frequency. According to Alzheimer the majority of such cases may be traced to syphilis, the later manifestations of which appear about this time. The disease runs its course with many epileptiform and apoplectiform attacks, with choreic disturbances and especially with paralytic phenomena, and ends rapidly in complete dementia. During the course of the disease, states of excitement and of confusion are (but rarely) to be observed while optic atrophy is common.

The great frequency of diverse pathological processes is indicated by the above consideration; but it must also be remembered that *the physiological sexual development is a critical period, requiring much insight and consideration from parents and teachers.* In the following pages will be given merely the principles of a rational hygiene for the periods of puberty.

So far as *nutrition* is concerned, the rapidly growing children at the age of puberty require an increased quantity of food, more than the amount necessary for adults. The latter have only to preserve their equilibrium by supplying the material that is used up; the corporal development of puberty, on the other hand, a great acceleration as it is over the growth in preceding years, which is shown by the gain of 10 Gm. instead of 5 Gm. daily, calls for an increased supply of food. According to Voit, Uffelmann and Ohlmüller, the average of food required daily consists of 70–90 Gm. of proteids, 20–50 Gm. of fats, and 500–250 Gm. of carbohydrates. Even though the capacity of the digestive apparatus at this time does not place any restriction upon the quantity or quality of the food-stuffs. Yet special consideration must be exercised in reference to the composition of the food. Of the special indications, the body weight is to be considered more than the age; moreover, abundant exercise in the fresh air is required with a diet that is mostly vegetarian. This fact is especially to be considered with those children that may have previously been accustomed to an abundant supply of proteids and fats, while for poorly nourished individuals a diet especially rich in fats is sometimes advisable. In all cases such animal food-stuffs as are rich in easily assimilated proteids, for example, milk, eggs, and cheese, are never to be placed too much in the background, especially in the diet of girls inclined to chlorosis. With boys, on the other hand, a diet too abundant in meats shows, at certain periods unfavorable effects upon their state of nervous excitability. To avoid this excitability it is advised that both sexes should abstain from sharp and stimulating articles of diet, such as mustard, large quantities of vinegar, strong coffee, tea, spices, and alcoholic beverages of any kind. Tobacco, of course, belongs also to the group of forbidden articles. It must be insisted upon that sufficient time be allowed for meals, especially in the case of school children. So far as evacuation of the bowels is concerned, children at puberty are of course to be trained in regular habits, if such habits have not been acquired at the proper time. A rational nutrition by means of a simple yet not monotonous diet is a necessary condition for normal development. Important for the attainment of the last-named end is the exclusion in *dress* of all articles of clothing that may interfere with the function of the respiratory, circulatory and digestive organs, such as narrow collars, belts, corsets and skirt-strings. The weight of the clothes is to be evenly distributed upon shoulders and hips. Both the skeleton, that is not yet perfectly firm, and the muscles,

not yet completely developed in strength, react very readily to injuries of any sort, with the production of such deformities as we have described above (page 120). Attention is to be paid to correct posture while writing, as well as sufficient light during work in the school or at home. Sitting down for long periods of time occupied with work requiring mental effort is an injurious factor of first importance at the time of puberty; and to combat this the temporary freedom from all work is often more rational than additional tasks that seem to suit the mental progress of the child. Increase of work requiring mental effort is to be regulated in this period solely by the progress of bodily development. Rational *division of time* between work, relaxation, and rest, with thorough use of the periods allotted to each, is very important in each case. While in general almost all the hours at school are devoted to the mental education, the attention to the physical development is relegated almost exclusively to the parental home, where private studies of all sorts in addition to the required school tasks lead to overwork of the brain, that is so sensitive during this period. In order that a race healthy in body and nerves may be raised, it is necessary to make changes in the above arrangement. The school must assign more time to compulsory physical exercise, while the requirements in mental work are to be correspondingly diminished, yet the fact must not be lost sight of, that systematic physical exercise is not necessarily equivalent to relaxation in all individuals. The various sports that have become so popular at the present time are valuable factors in opposing the injury done by the school, provided they are regulated according to individual capacities, and are not allowed to obtain complete hold of the sphere of mental interests. Excessive physical exercise can easily do harm in the period of puberty. While systematic gymnastic exercise strengthens the muscles, and exercise especially in the fresh air, by such means as rowing, swimming, cycling, skating, tennis and ball games produces good effect upon the capacity of the thorax by the increased expansion of the lungs, as well as upon the various groups of muscles and the general bodily agility, yet overfatigue may result with grave sequels in its train. Accordingly the duration and intensity of exercise is always to be carefully limited; this is especially true of cycling, which like other too strenuous exercises easily leads to overstraining the heart, ready as the latter is to break down at this period of development. Too prolonged a stay in cold water is especially to be forbidden to growing girls inclined to be chlorotic. Often not enough importance is attached to the hygienic value of a daily prolonged walk in the fresh air. The rational exercise of the body leads to a wholesome fatigue, which is made up for in the period of sound sleep. The latter is an especial necessity for individuals at the time of puberty, and care must be taken that its duration be perfectly sufficient and extend from 9 to 10 hours.

If we remember the necessity for sufficient sleep, and the various injuries that may be produced by nervous excitement, sensual stimulation, alcoholic excesses and the like, it becomes clear that individuals at the age of puberty are best prevented from taking part in the so-called social pleasures of any sort, unless, of course, the latter are made suitable, from every standpoint, to the stage of development of their age. In the sphere of education especial consideration is to be given to the nervous and mental life of such individuals. Individualized loving care and handling by considerate parents and teachers lead most children more easily and smoothly through this critical period, than the adoption of a strict routine, although at times energy and insistence ought to be displayed. It is important to keep guard over the reading matter, the amusements and the social intercourse of the child, while one of the tasks of a rational education nowadays is to furnish information in regard to the natural sexual processes. This may best be done by the parents themselves, with the use of examples taken from the life of plants and animals (Siebert). If the parents or teachers of the child are nervous themselves, very grave conflicts may occur at this time. In order to prevent such conflicts and to remove the harm that may be done by such bad example to the already sensitive nervous organism of the growing child, it is often advisable, from the physician's standpoint, to remove children, endangered in such fashion, from the school, or from their home, or even from life in the city, unfavorable as the latter often is in other conditions. In such cases, the boarding schools in the country are best suited to guide the child correctly in passing through the period of puberty.

Constitutional Diseases

DISEASES OF THE BLOOD AND OF THE BLOOD-PREPARING ORGANS

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PRELIMINARY REMARKS—PHYSIOLOGY

The microscopic blood picture in infantile blood diseases becomes intelligible only through knowledge of the normal blood in infancy.

The blood of the newborn infant exhibits the following peculiarities according to the latest publications of Schiff, Perlin, Carstanjen, Scipiades, and Takasu:

1. A very high specific gravity, 1.060–1.080, as against 1.050–1.060 in the adult.

2. A high percentage of hæmoglobin, 100 to 140 per cent. of the percentage in the healthy adult.

3. A specially large number of red blood corpuscles, 5,825,000–7,550,000.

4. An increased number of white blood cells, up to 36,000.

5. A preponderance of polynuclear cells, 73.4 per cent. polynuclear, 16.05 per cent. lymphocytes on the first day (Carstanjen).

6. Nucleated red blood corpuscles (as in the placental blood, where they are more numerous), up to the third day; up to the sixth day only in very few cases (Takasu), afterwards hardly any.

7. All these differences are considerable up to the fourth day, then they grow less; at the middle or end of the first month both hæmoglobin and number of red blood corpuscles have arrived at about the level of the adult man; the number of polynuclear leucocytes diminishes likewise and the percentage of the various kinds of leucocytes from the fourth day is about the same as it will be during the first few months.

No doubt some of the blood changes in the newborn are caused by the lack of water, considerable passing out through the intestines and perspiration, and in consequence of small supply.

In infancy there are also altered blood conditions as compared to the adult (Fig. 20, and Fig. 27, page 166), as follows:

1. Decreased amount of hæmoglobin down to 10.35 Gm., in the average 11.5 Gm. (as against 13–14 Gm. in the adult).

2. Often slight decrease of the red blood corpuscles.

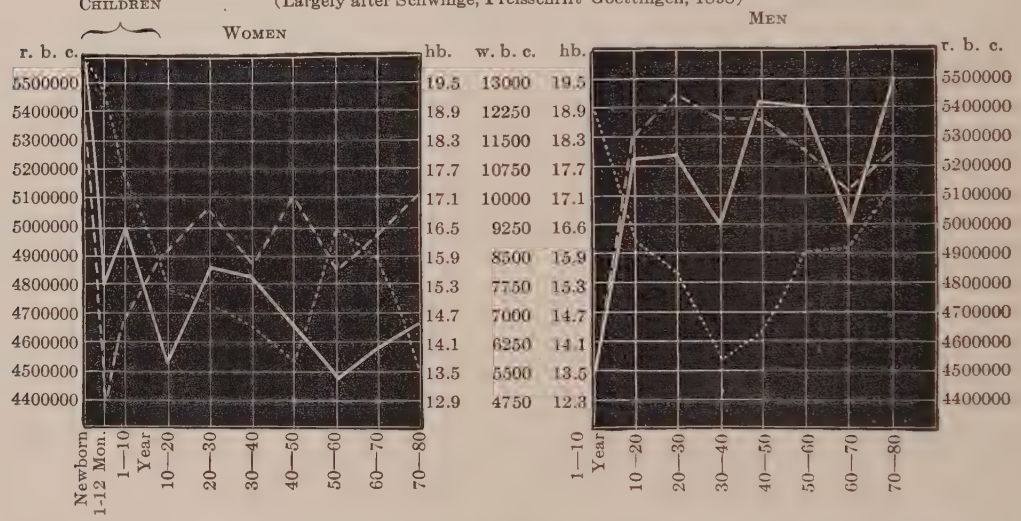
3. Increase of the white blood cells; about 12,000 to 13,000.

4. Preponderance of lymphocytes: about 50–55 per cent. The lymphocytes of infancy show greater differences in size than in the adult; there are also larger sizes. (These lymphocytes originate according to Ehrlich exclusively from the lymph-nodes; but according to

FIG. 20.

Curve of hæmoglobin (– – – –), of the red (——) and colorless (. . . . . .) blood corpuscles at various periods of age.

(Largely after Schwinge, Preisschrift Goettingen, 1898)



The curves show the exceedingly large quantities of hæmoglobin, red and colorless blood corpuscles shortly after birth, and the decrease after the first few days of life. The leucocyte curve remains almost during the entire first year above the height of later life, whereas the hæmoglobin and red corpuscles sink below and only gradually ascend again. After the fifteenth year the quantity of hæmoglobin and white blood corpuscles increases in the male sex and remains higher than in the female throughout life.

Grawitz, Walz and Pappenheim, similar cells exist also in the bone marrow.)

5. According to some investigators (Carstanjen, Karnizki) the so-called transitional forms are increased to about 8 or 10 per cent. (in the adult there are, together with the large mononuclear cells, only 2–4 per cent., according to Ehrlich-Lazarus).

6. Myelocytes (mononuclear cells with neutrophile granulation) are sometimes found in the healthy infant during the first few weeks of life, but always in slight numbers, never later (Zelenski-Cybulski).

7. Normoblasts are met with but rarely (Geissler and Japha, Zelenski-Cybulski, Karnizki), although formerly their occurrence even in healthy children was considered the rule.

From the second year the blood gradually approaches the normal blood of the adult, a state which is not attained, however, until the fifteenth or twentieth year. Up to the third to sixth year there is a preponderance of lymphocytes. Sex does not cause any material difference in the blood picture up to the fifteenth year.

Japha has not been able to demonstrate a proper leucocytosis of digestion in the bottle-fed infant, Gregor did not even find it regularly in the breast-fed infant. Moro found a decrease of leucocytes one-half to two hours after ingestion of food and seems to regard this leukopenia as a regular occurrence. If, however, a breast-fed infant was given cow's milk (heterogeneous albumin), there was an immediate occurrence of leucocytosis. Unfortunately the time of day when these experiments were made, is not stated. Besides, leucocytosis of digestion does not seem to be quite regular even in the adult, and the curve of leucocytes changes also during the day.

The blood-making organs of the infant are severely affected by disease. The infantile blood easily takes up myelocytes and nucleated red blood corpuscles (Zelenski-Cybulski). In infectious diseases the infant is perfectly capable of producing polynuclear leucocytosis. Measles do not produce leucocytosis (Felsenthal, Plantenga, Caccia, Tschistowitch and Schestakof). In whooping-cough hyperleucocytosis, with particular increase of lymphocytes was found even in afebrile cases (up to 47,000, de Amici and Paulioni, Cima). In severe cases of diphtheria Engel found 3.6–16.4 per cent. myelocytes. In intestinal affections of infants Schlesinger and others found lymphocytosis, Japha however was unable to confirm this.

SYMPTOMATIC ANÆMIAS INCLUDING SCHOOL ANÆMIA

Symptomatic anæmias deserve a separate discussion inasmuch as they depend so greatly upon their causes, and in many cases the recognition of the etiology (hunger, for instance) is equivalent to a cure. The blood picture is a resultant of the injurious influences acting upon the blood-forming organs and the reactive capacity of these organs: the weaker these organs, the more readily will anæmia be produced.

Anæmia after Hæmorrhage.—The cause of anæmia most easily recognized is hæmorrhage (from an umbilical wound, in consequence of melæna, infantile scurvy, epistaxis, hæmorrhagic diathesis, intestinal hæmorrhage, polypi, intussusception, gastric ulcer, intestinal parasites). If the acute losses of blood do not cause death, the infant will undergo rapid repair. Sometimes severe hæmorrhage is not followed by uninterrupted recovery, but may result in a prolonged and deleterious anæmia.

The therapy of acute anæmia requires, after checking the hæmorrhage, hypodermatic and intestinal saline infusions, heat, autotransfusion by lowering the position of the head and wrapping up the extremi-

ties, and finally administering nourishing, but easily digestible food. Iron therapy is not very important in acute cases of loss of blood, because the latter in itself incites the blood-forming organs to renewed activity, and the ordinary food should as a rule contain sufficient iron. Infants, however, should receive small doses of iron because milk is deficient in iron. Suitable preparations are ferrum oxyd. solub. (P. G.) 0.03–0.05 Gm. ($\frac{1}{2}$–1 grain) three times daily, ferrum lactic. (P. G.) 0.01 Gm. ($\frac{1}{6}$ grain) three times daily, liqu. ferri albuminat. (P. G.) 8–10 drops three times daily; it is important, however, that the organs of digestion be in good condition.

ANÆMIA AFTER ILLNESS (INCLUDING POISONING)

Another cause of anæmia may be disease processes and poisons. Poisoning by lead, arsenic, and mercury, is not of frequent occurrence in infants, but poisoning may happen through drugs in the administration of guaiacol, extract of male fern, potassium chlorate, pyrogallic acid, phenacetin, phenocoll, lactophenin. These substances either dissolve the red blood corpuscles or change the hæmoglobin into an inactive modification (*e.g.*, methæmoglobin). Of pathological conditions, the following, aside from those which lead to hæmorrhage: hæmoglobinuria, malaria, albuminuria, dysentery, other intestinal affections, infantile scurvy, sepsis and intestinal parasites (ankylostomum, bothriocephalus, trichocephalus, also ascaris, according to Demme). Congenital syphilis may be responsible for particularly severe anæmia (Loos), but not all cases of syphilis are anæmic, nor do they all become so during observation.

The many causes of anæmia make it incumbent upon the physician not to be satisfied with the diagnosis alone of anæmia, but to search for the cause. This includes a thorough physical examination; likewise an examination for intestinal parasites, which should never be neglected. In severe cases after purgative medication several stools should be thoroughly examined microscopically. Symptoms, course, and treatment of this form of chronic anæmia depend upon the cause.

ANÆMIA IN CONSEQUENCE OF MALNUTRITION, ETC.

Deficient or faulty nutrition is in infants a further cause of symptomatic anæmia; the somewhat complicated conditions are well described by Panum, Voit, Senator, Fr. Müller, Kieseritzky, and von Hösslin. Absence of iron in the food seems to have a particularly injurious effect (Ehrlich-Lazarus). The severest results are probably produced during the period of active bone-formation toward the end of infancy and during puberty. This also explains the anæmia of infants who have been fed too long on an exclusive milk diet. According to Bunge the newborn possess a comparatively large amount of iron; milk, however, is

very poor in iron, so that the amount of iron stored up will only last for a certain time, after which the deficiency of iron will make itself felt.

This form of anæmia cannot be cured by medication; the appetite should be stimulated and the necessary directions given for proper nutrition. Poor parents should be shown how the necessary quantity of calories, proteids and iron can be furnished in the cheapest way; to the rich it should be explained that lean meat alone is not sufficient as food, that an excess of proteids increases the internal work of the organism, that fat is by no means as injurious as is frequently supposed, that milk-fat (butter) can even be borne well, and that finally fresh vegetables and potatoes are very desirable food for children. The following table by Bunge shows the percentage of iron contained in a number of different food-stuffs:

100 Grams of Dry Substance Contain Milligrams of Iron:

White of eggs	Trace	Peas	6.2–6.6
Maize	1.0–2.0	Cherries, black, without stones	7.2
Peeled barley	1.4–1.5	Beans, white	8.3
Wheat flour	1.6	Carots	8.6
Cow's milk	2.3	Strawberries	9.3
Woman's milk	2.3–3.1	Lentils	9.5
Figs	3.7	Almonds, brown skin,	9.5
Raspberries	3.9	Cherries, red, without stones	10.0
Peeled hazel nuts	4.3	Hazel nuts, brown skins	13.0
Barley	4.5	Apples	13.0
Cabbage, inner yellow leaves	4.5	Cabbage, outer green leaves	17.0
Peeled almonds	4.9	Asparagus	20.0
Rye	4.9	Yolk of egg	10.0–24.0
Wheat	5.5	Spinach	33.0–39.0
Whortle berries	5.7	Pig's blood	226.0
Potatoes	6.4	Hæmoglobin	240.0

Milk and fine flour, and therefore also white bread, belong to the foods poorest in iron, whereas the opposite is true of spinach, asparagus, apples, cherries; also potatoes, peas and beans contain a fair proportion of iron. For this reason infants should not be fed too long on milk, not even mother's milk.

The presumably unfavorable influence of insufficient light and vicious air could not be proved by experimentation (Schönenberger, Flügge). It is possible, however, that in nervous children and those with a weak constitution, especially infants, this may be different. The evil effects of overheating, however, are well established (Flügge, Grawitz).

ANÆMIA OF SCHOOL CHILDREN

Various unfavorable influences are at work in the development of school anæmia. Vitiated air may cause a bad effect by acting on the nervous system and thus causing disgust in tender children; overheating is also a factor, especially if the heat is supplied from a central furnace;

further, exertion, purely psychic causes, longing for the mother, ambition, anxiety; finally the lack of fresh air may well be of greater importance than the presence of bad air. Some children become affected in the first six months of their school work; others only in later years, as increased studies make greater demands upon them. The children of the poor are distinctly more affected in large cities than those of the rich. This is even more so in children of widows, which is explained not only by unfavorable surroundings, but also by unsuitable psychic influences on the part of the mother. Here, as in all forms of anæmia, hereditary tendency and especially nervous debility play a considerable rôle; illness or advanced age of the parents at the time of birth of the children, tendency to migraine and similar disturbances, favor the development of school anæmia and make its cure more difficult.

Symptoms.—The subjective complaints and nervous troubles are fatigue, heaviness in the legs, headaches which occur principally in school, vomiting at school which in severe cases may be repeated almost daily. Especially after bodily exertion, such as gymnastic exercises, there is pain in the sides and epigastric region. Parents notice the depressed condition of the child, the decreased vitality, increased desire to sleep, and diminished inclination to take part in games. Sleep is restless and often disturbed by attacks of pavor nocturnus. There is less appetite (the lunch is brought back home), and the bowels are irregular.

The objective signs are: weakened constitution, pallor of the formerly fresh complexion and mucous membranes, decrease of the subcutaneous fat and a striking flabbiness of the muscles. Respiration and pulse are frequently accelerated, the pulse may be full, but soft. Examination of the blood shows a decrease of hæmoglobin and of red blood corpuscles; sometimes the latter show differences of form, also a slight increase in leucocytes; usually the changes are not very pronounced or they may be absent altogether in spite of severe clinical symptoms.

Cardiac dulness is sometimes slightly increased; the impulse may be widened and surprisingly strong. Heart murmurs are found, especially after slight exertions, and the first sound may be reduplicated or impure, or accompanied by a slight murmur. Over the cervical veins a venous hum may be distinguished even in infants.

Many otherwise robust children, who are at once affected in their first school year by the mere change of conditions, or perhaps later owing to unfavorable exterior influences, recover rapidly after a short vacation; others, if once affected, may drag the trouble with them throughout their school life. These are usually weak children with an hereditary taint. In cases of this kind the prognosis is doubtful in view of the tendency of the debility to persist until a later period of life. These children are also apt to develop scrofula.

The **diagnosis** requires careful exclusion of other affections (scrofulosis, tuberculosis, intestinal parasites).

Therapy.—The necessity of removing the original cause would make it desirable to keep the children away from school for a time. In serious cases this should always be done, as the injurious influences which act on both body and mind are thereby counteracted. In the first stages of the trouble a few weeks' rest is frequently sufficient, but in a case of long standing prolonged rest is required. After recovery has taken place, it is generally easy for the refreshed brain to make up for lost time. In obstinate cases where the school again and again causes the trouble to break out afresh, a cure should be attempted in spite of the child attending school. Well-to-do families may for a time have recourse to private lessons. For the poorer part of the population schools situated in the woods are excellent in this respect. It is important to correct mistakes of education at home, to tone down the ambition of the mother in wishing her child always to be the first, to omit the music lesson, etc. Among the poor too much house work (see the Care of Children in Poor Families); or using children for business purposes such as delivering newspapers, are also great exertions and shorten the hours of sleep. The time out of school should be largely devoted to sleep, also during the day a few hours of sleep should be inserted, perhaps immediately after school or before dinner. Children should be in the fresh air as much as possible. The arrangements which permit children, including the poor, to spend at least a few weeks of the year in really good air, are to be hailed with delight. Places of recreation, vacation colonies, sea resorts, summer colonies and rural sanitaria, or possibly a visit with relatives in the country, are desirable. Even if after return to town the body weight and percentage of hæmoglobin should fall again, in the majority of cases an improvement still remains as compared to the condition before the commencement of the cure. The children of well-to-do parents are sent to rural sanitaria or summer resorts. The best places are those where the climate is warm and yet affords sufficient protection from excessive heat. In the country, heat is much more bearable than in the streets of great cities, where the gigantic piles of stone and mortar absorb the heat of the sun and do not easily become cool again. Anæmic children can bear heat better than cold, and summer resorts in the flat country are very suitable, also watering places (there is no necessity for taking the baths), whereas many places in wooded districts have too many cold and wet days. The climate near the sea has an evil reputation in regard to its effect upon anæmic patients. Those endowed with a fairly good power of resistance may be sent to the seaside, but care should be taken not to expose them to the hot rays of the sun and not to allow them to bathe in the sea. With many young children the climate at high altitudes agrees well, which in the opinion of very

competent physicians may have a salutary effect in very obstinate cases. Very high altitudes, however, are not suitable for every child. High altitudes probably act less by the increase of red blood corpuscles, than by improved metabolism (Miescher, Loewy and Zuntz, Schumburg and Zuntz, Meissen and Schroeder, Gottstein). As to the use of chalybeate waters, which may also be used in the case of young children, more will be said in a subsequent paragraph.

Hardening of the body is only justified where overanxious parents pamper the child; otherwise anæmic children require indulgent care. They should not be persuaded to take long walks or to play games which require much exercise. Gymnastic exercises, which frequently cause trouble, should be discarded. After the requisite degree of strength has been gained, which is well indicated by the gain in body weight, it is advisable to take brisk walks even in cold winter weather, and to warm the hands and feet by brisk movements at play. Then also gymnastic exercises are indicated. Swimming or cold frictions frequently exacerbate the trouble considerably, because the child is not nourished well enough to stand the loss of body heat, so that no reaction of the vessels takes place. In these cases it is better to prescribe friction with coarse towels which are gradually and carefully replaced by rubbing with eau de Cologne or brandy and finally by a wet sheet. The child should be rubbed immediately on being taken out of the bed, and afterwards be placed back into bed for a few minutes. Rubbing may also take place after a warm bath, but the chief concern is that the child invariably be warm after the treatment. Later on it is well to let the children splash about with their feet in cold water. Many authors recommend sweat baths in the case of very young chlorotic children.

Great attention should be paid to sufficient nutrition. Five meals should be kept up. Before getting up in the morning and in the evening some milk may be given to the child in bed. Before going to school the child should partake of a proper meal containing plenty of albumin (milk, buttered bread, and if possible, egg or meat). Then also the second breakfast will usually be eaten, and in many schools provision is made for allowing the children a glass of good cool milk. Before dinner rest is desirable. Generally speaking, the child may eat whatever it likes, so long as it eats.

Personal taste may be gratified by allowing caviar, small quantities of sardines, ginger, pickled melon; older children may have a piece of herring, sardines, cucumbers, salads which may be dressed with lemon (beans, tomatoes, celery, asparagus, endives, green salads; in dressing leaf salads great cleanliness should be observed). By these dishes and plenty of sauces, and by coating meat dishes with fruit jams, meat can be more easily administered. In the case of younger children who cannot masticate well, the meat should be cut into very small pieces or

mashed. For this purpose meat cutting machines, scissors, masticators, etc., have been invented. Food containing a high percentage of iron is preferable (see Table on p. 135). Vegetables can be cooked very nicely with butter, cream is also well borne, especially with strawberries (caution on account of decomposition after standing); many children are fond of linseed oil (with potatoes). For "fattening" may be recommended, oatmeal, red grits, jellies; honey is very nutritious (1 tablespoonful equal to 75 calories). Older children are given for a few weeks (only to stimulate the appetite) a little wine (sweetened claret, a liquor glass to half a wineglassful twice a day), a glass of malt beer (2–3 per cent. alcohol, 7.5–10 per cent. malt extract).

Proprietary foods should only be given if the ordinary food cannot be administered in sufficient quantities. Only few fat preparations are suitable for continued use; oil of sesamum and codliver oil (twice daily a teaspoonful to a tablespoonful), the latter also in the form of ossin strochein (a combination with the egg albumin, in tablespoonful doses) also effervescent oil are generally well liked. Moreover, chocolate or cocoa containing oleic acid is well assimilated according to Zuntz, and finally lipanin (olive oil with 6 per cent. oleic acid, in teaspoonful to desertspoonful doses) though this is expensive. Of carbohydrates may be mentioned: oats-cocoa, Theinhardt's hygiama, malt extract (50 to 55 per cent. sugar, 10 to 15 per cent. dextrin, 5 per cent. albumin, 1 tablespoonful of 20 Gm. is equal to 60 calories), also to be recommended as a mixture with milk is Löflund's maltsoup extract, or crystallized (Brunnengräber) with 83 per cent. carbohydrates, 5 per cent. albumin; 1 tablespoonful equals 85 calories); of albuminoid preparations: puro (meat juice with 33 per cent. albumin, 19.16 per cent. extract); of milk albumin preparations: plasmon (cheap), nutrose, sanatogen, with 80 to 90 per cent. albumin, the latter also with 5 per cent. glycero-phosphate of sodium, all soluble or miscible in cold water; also the inexpensive roborat with 94 per cent. vegetable albumin, free from nuclein, miscible in water, suitable for mixing with flour for making bread (up to 40 per cent.) somatose (albumose with 80 per cent. of soluble albumin) is also on the market in liquid form, it is expensive and in large quantities causes diarrhœa. Generally albuminous preparations are not liked for a long-continued period, but have the great advantage of containing albumin in concentrated form. Meat juice (freshly made with Klein's meat juice squeezer, also on the market as Valentine's meat juice, etc.) and meat extract may be given as appetizers, but have little nutritive value.

Medicinal therapy can only be attended with success, if the entire hygienic measures have been regulated in accordance with the principles laid down above. At all events the administration of iron for several weeks in succession is always advisable as soon as anæmia has once been established.

In older, flabby children arsenic sometimes produces good results; the dose is to be gradually increased and correspondingly decreased.

Not infrequently there is a complication of scrofula which has to be treated according to the usual methods. Medication:

Syr. ferri iodidi (to be kept from the light) 15–25 drops three times daily (from the fifth year).

Headache, want of appetite, constipation, generally give way to the hygienic measures mentioned above. For headache 0.25–0.5 Gm. (3½–7 grains) antipyrin may be given. The appetite should be stimulated by bitters, such as:

Tr. chinchonæ comp., ½–1 teaspoonful three times daily (5–7–15 years) in ½ wineglass of sugar water, ¼ hour before eating; tr. rhei aromat., ½ teaspoonful, same way.

The following is also good:

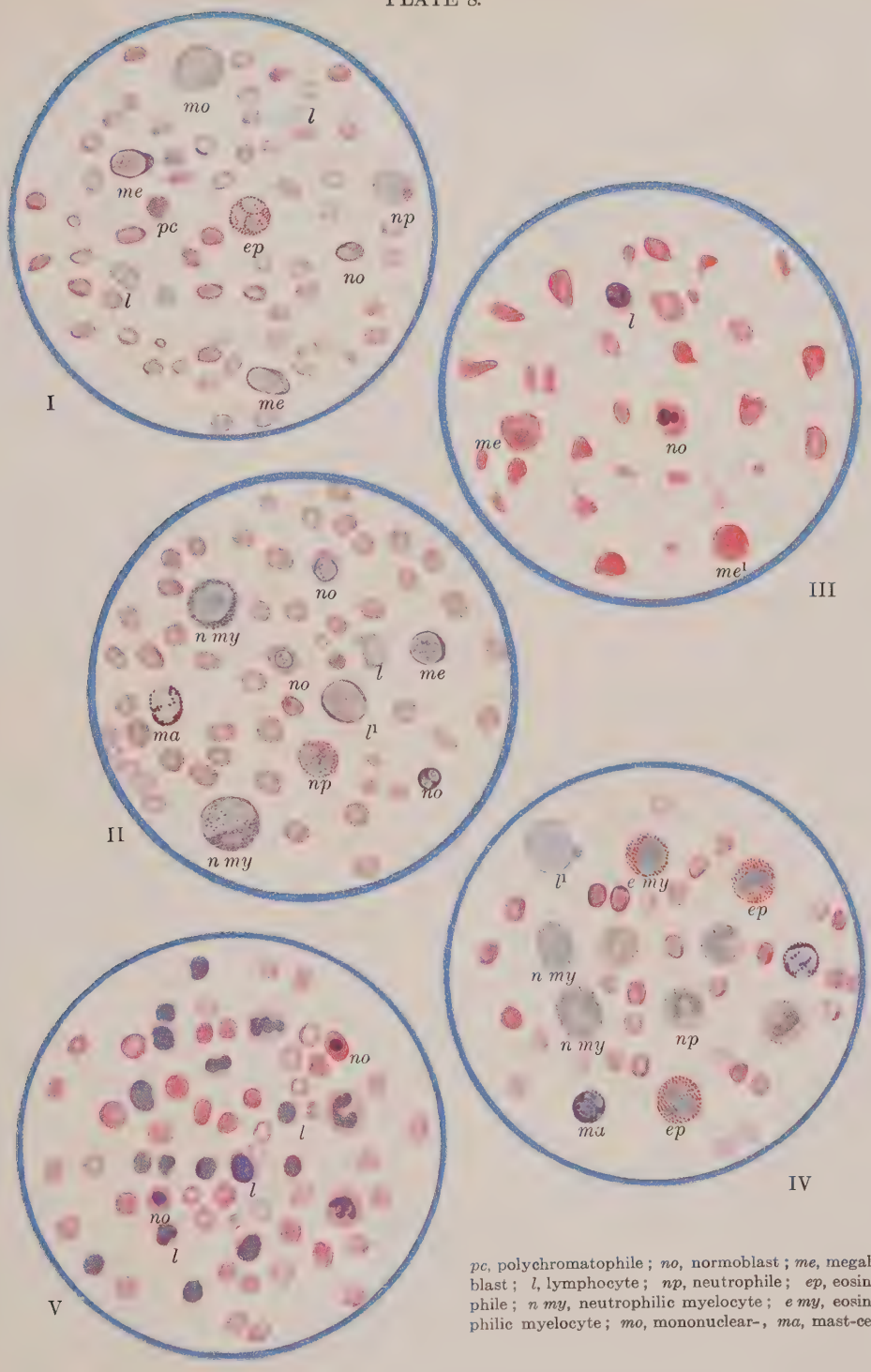
Fellow's syrup three times daily ⅓–½ teaspoonful (5–9–12 years) in ½ wineglass of water, then orexin in chocolate tablets of four grains, several days once or twice two hours before meals.

Constipation may be benefited by just taking a walk especially in children with weak muscles; useful, however, are gymnastic exercises, bending of the body (with caution at time of menstruation), breathing and arm exercises, and massage by a skilled operator. A glass of cold water should be taken in the morning on an empty stomach, baked prunes, also coarse food (brown whole meal bread), buttermilk, kefir two days old, gingerbread, malt extract (very useful; 1–2 tablespoonful daily). Care should be taken to maintain good nutrition, psychical influences should not be overlooked, for even young children may be pronounced hypochondriacs. Regular habits should be inculcated, daily at the same time, the best time being immediately after rising or after the first breakfast. In the beginning, artificial help should be resorted to by an enema of a pint of water, two ounces olive oil, or an injection of 1–2 teaspoonfuls of glycerin with double or treble the quantity of water. Medicinally may be prescribed:

Pulv. glycyrrhizæ comp. ½–1 teaspoonful; pulv. rhei. comp. by the knife point; confection of tamarinds (in 1 piece 0.5 senna), ab. ¼–½–1 confection; fluid extract rhamni purshianæ, 2–3 times daily 10–20 drops in water (bitter); California fig syrup (1 tablespoonful contains 3.11 senna) one teaspoonful three times daily; extr. aloes, extr. rhei. aa f. pil. 1–2–3 pills. (older children).

ANÆMIAS AT THE END OF THE NURSING PERIOD, INCLUDING ANÆMIA PSEUDOLEUKÆMIA INFANTUM

Nature and Name.—Among the wretched children who suffer from intestinal disturbances, rachitis, etc., and have not the physical strength of healthy children, there are always a number who, after the period of



pc, polychromatophile; *no*, normoblast; *me*, megaloblast; *l*, lymphocyte; *np*, neutrophile; *ep*, eosinophile; *n my*, neutrophilic myelocyte; *e my*, eosinophilic myelocyte; *mo*, mononuclear-, *ma*, mast-cell.

I. Anæmia pseudoleukæmia.—Fixation, 1% formol-alcohol; stain, aqueous eosin sol., then aqueous methylene blue sol. Erythrocytes of different size and form, many normoblasts, megaloblasts, and mononuclear cells. Reds, 1,784,000; whites, 30,200.

II. Anæmia pseudoleukæmia. Stain, May-Grünwald.—Light poikilocytosis, many normoblasts and megaloblasts, two neutrophile myelocytes, one mast-cell.

III. Anæmia perniciosa in adults. Stain hæmatoxylin and aqueous eosin sol.—Marked poikilocytosis, megalocytes (me^1), megaloblasts, leucocytes diminished.

IV. Chronic myelogenous leukæmia (7-year-old boy). Stain, May-Grünwald.—Great increase of all nucleated cells with differences in size. One giant lymphocyte (l^1). Reds diminished.

V. Acute lymphatic leukæmia (13-year-old boy). Stain, hæmatoxylin and aqueous eosin sol.—Great increase of lymphocytes of different sizes, few polynuclear cells, few normoblasts.

nursing has come to an end, are conspicuous because of their pale complexion. The majority of these cases are cured after a shorter or longer period, but in some cases the gravest clinical manifestations develop. All these cases, however, have so many points in common by their time of origin at the end of the nursing period, by their pathogenesis and not in the least by the possibility of a favorable course even in grave blood changes, that it seems justified to consider them in one common group.

The graver cases are frequently grouped under the name of splenic anæmia which Italian authors (Somma, Jemma) have given to this symptom-complex on account of the simultaneous enlargement of the spleen; or it is called pseudoleukæmic anæmia. This name was proposed in 1889 by von Jaksch to designate a pathological picture characterized by oligocythæmia, oligochromæmia, considerable permanent leucocytosis, enlarged spleen, slightly enlarged liver and sometimes also enlarged lymph-nodes. The term, however, is not very happily chosen, because pseudoleukæmia is even characterized by the absence of increased leucocytosis.

Italian authors and also a number of Germans (Fischl, Geissler, Japha) include the grave infantile anæmias in the secondary anæmias with a toxic basis, while others regard them as a genuine blood disease (Audéoud), practically as a middle condition between anæmia and leukæmia. Evidently, different authors have described different conditions under the same name. Cases that die under a progressive increase of leucocytes should perhaps be classed as leukæmia from the beginning. Some authors (Weil and Clerc, Lehndorff) prefer to separate cases with considerable increase of myelocytes (in Lehndorff's case 1.3–12.7 per cent.) as essentially a blood disease (perhaps infantile leukæmia). True, in Lehndorff's case the organs harbored myeloid foci, but there are cases with numerous myelocytes (6.5 per cent. in the case mentioned later on) whose blood findings may become normal again, and the possibility of a favorable termination is rather a point which might induce us to include these cases of infantile anæmia. It is a difficult question whether anæmia pseudoleukæmica represents the pernicious anæmia of childhood which under the changed conditions of childhood shows a somewhat altered blood picture. In this respect the observations made by Reckzeh are of special interest, that the influence of blood poisons in young animals produces a blood picture which, by the large number of normoblasts and leucocytes, resembles that of pseudoleukæmic anæmia, whereas in full-grown animals the picture of pernicious anæmia is the result. It is questionable, however, whether the conditions of the animal organism can be applied to the human one.

Etiology.—At no age are there so many anæmias with relatively grave blood pictures as at the end of the nursing period, say from the seventh month to the end of the second year. It may therefore be as-

sumed that at this particular period there must be a predisposition for this sort of affection. This functional deficiency in the blood-forming apparatus is analogous to the peculiar affections of the osseous and nervous systems, rachitis and tetany, which likewise occur at this period. Among the immediate causes there are in the first place artificial nutrition and its sequelæ, nutritive disturbances and intestinal catarrhs (in breast-fed children serious cases hardly ever occur), unsanitary and unhygienic domestic conditions. Also in well-to-do families children become affected if, for fear of catching cold, they are kept in badly ventilated rooms. Premature children are particularly exposed as well as children who have not completely recovered from some hæmorrhage (umbilical hæmorrhage, melæna). The statement that tuberculosis (Raudnitz) and syphilis exert a predisposing influence is not to be wondered at, but in all the cases observed by the author these affections have not been established with certainty, nor are grave anæmias a particularly frequent complication of syphilis. The spleen cannot be the primary pathological focus and can hardly have anything to do with the regeneration of the blood, since its enlargement becomes frequently reduced before the blood picture has become normal, while the extent of the enlargement does not always correspond to the gravity of the anæmia. Generally deficient new formation of blood seems to constitute the nature of the affection. Simultaneously there may under certain circumstances be an exaggerated destruction, but there are only a few cases in which the anæmic (granular) degeneration of the red blood corpuscles is found as positive evidence of the effects of a blood poison.

FIG. 21.

Anæmia pseudoleukæmica infantum. Severe rachitis with considerable thickening of the epiphyses of the lower arms and legs, considerable bending of the lower arm and thigh, considerable thoracic deformity, frog belly, widening of the inferior thoracic aperture; spleen with distinct incisure reaches to the symphysis; liver not particularly enlarged.

Pathological anatomical findings exist only in limited numbers even of the severer cases of anæmia. In these cases the spleen is either

hard or soft according to whether the stroma or parenchyma is the more affected by the hyperplasia. There is nearly always slight swelling of the lymphatic glands, and among the complications there is chiefly bronchopneumonia. Luzet and Lehndorff, whose case may perhaps have to be classed as leukæmia, found red bone marrow, the former also cells in the hepatic parenchyma which he regarded as precursors of red blood corpuscles. Lehndorff found myeloid foci in the liver and kidneys.

Fig. 22.

Anæmia pseudoleukæmica. Girl, 14 months old, boy 16 months old, both rachitic, the girl a syphilitic suspect. Enlarged spleen with but slightly enlarged liver. In the case of the boy the incisure of the upper margin is very distinct.

Blood-pigment deposits which are demonstrable in all primary blood destruction, were absent.

The **symptoms** depend upon the gravity of the anæmia. In milder cases there are no particular complaints except a gradually increasing pallor and the child, which does not thrive and is usually rachitic, may be quite vivacious. In severer cases the pallor increases and assumes a yellowish tint; the child becomes weak, ill at ease, peevish, lies down listlessly, and answers every attempt to change its position with pitiful crying. This is to a large extent occasioned by severe rachitic changes, and besides there are often intestinal disturbances, and a large percentage suffer from bronchopneumonic affections following an exceedingly

chronic course. In cases of this kind there are also febrile manifestations. Frequently there are slight hæmorrhages in the skin and mucous membranes, less frequently on the surface, especially epistaxis. Retinal hæmorrhages are hardly ever observed even in severe cases.

Fig. 23.

Acute (♀) and chronic (♂) leukæmia. Boy, 7½ years, sick for months, beginning with distention of abdomen and pain, infantilism, hard enlarged spleen, slightly painful on pressure, smooth, gradually increasing, only temporarily reduced by the application of X-rays. Hæmoglobin 30–35 per cent. Erythrocytes 3,810,000, leucocytes 261,500, L. : E. 1 : 14.5. Blood picture (Plate 7,) almost exclusively granulating cells, among which are found mononuclear ones in large quantity. General condition not serious, boy out of bed lively. Leukæmic retinitis.

Girl, 3 years, became affected a few weeks ago, beginning with abdominal complaints, inability to walk, enlarged spleen somewhat softer than above, deeply notched, of changeable size. Grave general condition, hæmoglobin (Fleischl) 30 per cent., E. 2,800,000, L. 1,250,000, L.: E. 1: 2.5. Large mononuclear granulated cells, mucous membranes slightly discolored, hæmorrhages from nose and skin, also from vitreous body, grave bilateral leukæmic retinitis. Both children still under treatment.

Among the objective signs in severe cases there is always an enlarged spleen, but under certain circumstances only so slightly enlarged that it does not reach beyond the costal arch by more than 1 to 1½ finger's breadth, in other cases the spleen may reach down to the iliac crest and extend by several fingers' breadth beyond the median line, so that its outlines are distinctly visible through the flabby abdominal wall when the child lies on its back. On palpation the organ feels strikingly hard and the incisure of the upper margin may often be felt distinctly. As a matter of course these enlargements distend the abdomen considerably, widen the inferior thoracic aperture and disturb the movements of the thoracic organs. The liver is seldom much enlarged, but if it does extend by two fingers' width beyond the costal arch, it generally feels soft. Much swelling of the lymphatic glands is seldom present, but nodes the size of a pea or bean are often felt in the neck, axillæ and in the flexures at the elbow and groin.

The blood findings (see Plate 8, Figs. 1 and 2) vary according to the degree of the anæmia and show in various cases every gradation to the severest lesions. In mild cases there is hardly more alteration than a diminution of the hæmoglobin, which may be followed later by a more or less important diminution of the red blood corpuscles. The hæmoglobin quotient of the red blood corpuscles is diminished. As the anæmia progresses, considerable differences in the size of the red blood corpuscles are noticeable, forms but slightly indented, also here and there nucleated cells of normal size (normoblasts). The white blood corpuscles in mild cases without complications are but slightly increased beyond the normal number for the infantile period (10,000 to 20,000); the percentage of the lymphocytes corresponds about to the normal proportion for the first year of life. In the severest cases which are also classed as splenic or pseudoleukæmic anæmia, as explained before, the hæmoglobin may sink to 30 per cent. of the normal and lower still, the number of red corpuscles to below a million. The amount of hæmoglobin contained in the separate red blood corpuscles may vary considerably. The specific gravity may be materially reduced and the tendency to nummular formation may be absent. The red blood corpuscles exhibit considerable differences in size from dwarf to giant proportions, sometimes there is a pronounced poikilocytosis, polychromatophilia and in isolated cases granular degeneration. Nuclear forms are sometimes met with in such large quantities as hardly in any other blood affection, up to 20,000 in a c.mm. (Lehndorff), figures of many thousands are not rare, and as many as 25 per cent. may be megaloblasts. There is a considerable increase in the colorless blood cells up to 50,000, in fact, cases have been reported with initial leucocyte counts of 114,510 (Jakœch) and 122,222 (Baginsky) which have been cured. The increase concerns rather the mononuclear form, so that the percentage of polynuclear neutrophile cells (30–40 per cent.) may well appear diminished against the normal infantile figure; the proportion, however, is subject to changes. Besides, very frequently some neutrophile and eosinophile myelocytes are met with in cases which are likewise susceptible to improvement. "Mastzellen" exist only in small quantities. Often there are strikingly large cells with round, stainable nuclei and abundant, coarse, weakly basophile or homogeneous protoplasm which is also stainable by eosin.

Nuclear segmentations occur frequently, especially in the nuclear red blood cells, but also in the white cells, and they can be well seen in the Zeiss chamber in a blood diluted with a 1 per cent. acetic acid. In making dry preparations, they are generally crushed.

The following table contains the proportionate figures of 2 cases. In the first case (Fig. 21) the blood picture improved considerably by clinic treatment; death ensued later during home treatment, probably

from bronchopneumonia; the second case was completely cured in the Children's Asylum of the City of Berlin (Finkelstein); the child made splendid progress, but died later of whooping-cough and pneumonia.

	Number of leucocytes.	Polynuclear leucocytes.		Mononuclear leucocytes (myelocytes)		Large mononuclear and transition forms.	Large and small lymphocytes.	Mastzellen.	Neutrophile dwarf blood corpuscles	Free nuclei.	Normoblasts.	Megaloblasts.	Nuclear segmentation.
		Neutrophile.	Eosinophile.	Neutrophile.	Eosinophile.								
Case I ...	30,200	34.0	4.9	5.0	1.5	1.6	49.0	0.6	0.6	4.	1: 2.5 leucocytes	1: 20 leucocytes	Large quantities.
Case II ...	14,000	40.0	3.8	4.9	0.4	3.2	48.6	...	...	...	1: 5 leucocytes	1: 22 leucocytes	.....

Course and Prognosis.—In mild cases the anæmia soon improves under proper treatment; in severe cases, especially if external injurious influences cannot be removed, it persists for months and may result in death, generally in consequence of complications, usually of bronchopneumonia. Mild cases of infantile anæmia should also be taken seriously, because the transition to severe forms is never impossible, and at all events under insufficient treatment a long-continued debility may remain behind. On the other hand, even in severe cases the prognosis need never be pessimistic, as even the gravest blood conditions may undergo a surprising improvement under appropriate treatment.

The **diagnosis** itself offers no difficulties. The differentiation from pernicious anæmia is possible through the enlargement of the spleen and the increase of leucocytes, while in pernicious anæmia the leucocytes decrease. Sometimes, however, the differential diagnosis from leukæmia is by no means simple. For splenic anæmia speaks (1) the number of leucocytes, which seldom exceed 50,000; (2) the practically sustained percentage during the first year of the various kinds of leucocytes in spite of the presence of myelocytes, with a possible slight preponderance of lymphocytes; (3) the considerable changes in the red blood corpuscles, especially the enormous quantity of nucleated red corpuscles. The comparatively small size of the liver (von Jaksch) is not quite a reliable sign. Doubts may exist particularly if a polynuclear leucocytosis complicates the anæmia, because in that case the blood picture sometimes resembles myeloid leukæmia.

The best **prophylaxis** is naturally nourishment from the mother's breast. Artificial nutrition should be made as rational as possible. It is not proven that a particular food, such as buttermilk, specially favors the development of severe anæmias, but any such food had better not be continued too long. The same refers to the feeding with sterilized preparations. Of importance is proper regard for light and air, even in winter.

Treatment.—The first step in the treatment is to correct errors in diet and to remove intestinal disturbances. Of importance in many cases is feeding with mixed diet, such as a few teaspoonfuls of spinach, mashed carrots, mashed potatoes, asparagus tips, artichokes, cauliflower, fruit juice (preferably raw), also meat juice, broth, and the exclusion of oversterilized or pasteurized foods. The appetite is stimulated by the administration of bitters (tr. cinchonæ comp. or tr. rhei vinos., 8–10–12 drops in sugar water three times daily) or a mixture of pepsin and hydrochloric acid (1:2:100). Great care should be taken under any circumstances to provide good light and air. Children of poor parents are now best cared for in children's hospitals. If the weather conditions are favorable, infants are allowed to lie in the open air or on verandas. Children living in cities are highly benefited by removal to a dry, sunny spot in the country; a great improvement is rapidly produced in the case of poor children by sending them to the garden colonies of larger cities; better still may be the effect of a mild sea climate, or southern climates in winter. Of great importance is the care of the skin; it should be rubbed with flannels and spirits of calamus several times every day, while every other day a warm chamomile bath or one prepared with a decoction of calamus should be given. Washing with cold water should be avoided. At the same time direct medicinal treatment may also be tried. Rachitic children are given phosphorated codliver oil to improve the anæmia (phosphori 0.02, ol. jec. aselli ad. 100.0, one teaspoonful in the morning after the first meal, in all about three bottles), which is a suitable combination and apparently quite efficacious. Of iron preparations the following are suitable for infants: liquor ferri alb., 8–10–15 drops three times a day; ferri lact. 0.03–0.05 Gm. ($\frac{1}{2}$–$\frac{3}{4}$ gr.) three times a day; ferri pyrophosph. c. ammon. citrico, 0.05–0.1 Gm. ($\frac{3}{4}$–$1\frac{1}{2}$ gr.) in mixture three times a day, but iron may also be dispensed with. Arsenic is sometimes not borne well; in some cases, however, the use of greatly diluted solution (sol. Fowleri gtt. 2, water 50.0 Gm. (14 drams),4–5 teaspoonfuls a day, for a child of 2 years) has been followed by remarkable improvement. Heubner recommends a teaspoonful of fresh bone marrow three times a day, stirred up with egg or spread on bread; d'Orlandi recommends 25 Gm. (7 drams) daily of fresh spleen juice.

CHLOROSIS

Chlorosis is an anæmia which attacks almost exclusively the female sex in the period of development and in the decade following; its origin may, however, frequently be traced to early childhood.

Nature and Etiology.—Greatly varying theories have been advanced on the nature and etiology of this affection. One mistaken idea was that it owed its existence to a disturbed resorption of iron (Zander), to an intoxication from the intestine (Duclos), perhaps in consequence of the usually prevailing constipation; Grawitz attributed the cause to a

primary disturbance in the formation of lymph, rendering the blood watery and swelling up the red cells; von Noorden considered a disturbance of the inner secretions of the sexual organs the cause of the functional weakness of the blood-making organs; Rosenbach and Meinert hold that the corset impedes respiration, displaces the abdominal organs, and thus leads to nervous and functional disturbances. Virchow pointed to a constitutional cause. In individuals who have shown signs of chlorosis during life, he found hypoplasia of the vascular system (stenosis of the aorta, thinness of its walls, anomalies of the vessels). Even if all cases of chlorosis do not present these grave irreparable changes, the origin of the affection is nevertheless probably attributable to a constitutional weakness in the majority of cases. This view is supported by the distinct heredity of the affection. This weakness may lead to disturbed blood formation during the period of development, and then only in the female, such disturbance being characterized by the fact that the cells do not sufficiently assimilate the iron. The fact of its occurring principally in the female has its analogy in the occurrence of Basedow's disease at the same period. This fact also supports the opinion of von Noorden who looks upon the affection as a disturbance of the internal secretion of the sexual organs.

Its occurrence may be favored by all such factors as may be regarded as causes of secondary anæmia: insufficient food supply, vitiated air of school rooms, and—in no small degree—the objectionable distribution of school time, excessive study, insufficient recreation and sleep; in older children mental excitement through homesickness, worry, anxiety, ambition and improper literature. Excessive masturbation is probably much more to be regarded as a sign of a debilitated constitution than as a cause of injurious effects.

Symptoms.—The blood changes in chlorosis are characterized by the fact that the hæmoglobin is disproportionately decreased to a much higher extent than the number of red blood corpuscles (Duncan). According to Graeber 7 cases out of 28 had more than 5,000,000 red corpuscles, 13 cases 4 to 5 millions. A reduction of the red corpuscles by one fifth corresponds to a sinking of the hæmoglobin by one half. For this reason the red corpuscles look pale and are of unequal size. In severe cases poikilocytes and normoblasts may finally make their appearance. The white blood corpuscles are, according to reliable authors, on the whole, normal, so far as their number and proportion are concerned. The specific gravity sinks about in the same proportion as the percentage of hæmoglobin. It should be remarked, however, that the blood changes do not in all cases keep step with the clinical symptoms; sometimes it is a matter for surprise to find the palest complexion associated with quite a sufficient percentage of hæmoglobin, or even no blood changes at all, in spite of pronounced clinical symptoms.

Nervous troubles are the dominating factor of the disease picture. In the foreground stands lassitude. In mental or bodily exertions there may be flickering before the eyes, paroxysms of vertigo and spells of fainting. The feebleness often stands in no proportion to the blood changes, sometimes it is only pronounced in the morning hours, while even greater exertions can be borne in the evening. Anomalies of disposition, inclination to ponder over things, sensitiveness, are of frequent occurrence. There may be pain in the epigastrium and in the sides probably owing to muscular weakness; palpitation of the heart occurs in paroxysms as in true tachycardia. Disturbances of the vascular innervation are also frequent, such as changes of the complexion, cyanotic extremities, continuous tormenting feeling of chills, tendency to chilblains in winter. Headache, too, which occurs partly as a continuous dull pressure and partly as paroxysmal migraine, may to a certain extent be based on disturbances of vascular innervation. Dyspnœa is frequently caused by visibly unskilful and far too flat respiration. Complaints about digestion, pains in the stomach, anorexia, constipation, always play an important rôle; less frequent are peculiar cravings (pica) as for instance for eating chalk, coffee beans and soured food.

The numerous complaints correspond comparatively little with the bodily manifestations. The color of the skin and mucous membranes is always pale. The state of nutrition may be good; but on the other hand there are frequent cases of badly nourished, chlorotic young women, especially in poor families if its beginning dates back to early childhood. In such cases a general enteroptosis is frequently met with, also in girls who do not wear stays, also in boys, although less frequently. The enlargement of the spleen described in chlorotic cases (45 per cent. according to von Noorden) is probably to be regarded as partly due to sinking.

As stated above, Virchow looked upon the cause of chlorosis as a hypoplasia of the vascular system. Pronounced cases of this kind always furnish a distinct pathological picture which is not difficult to diagnose (Fräntzel). They generally occur in persons of tall and slender build with but slightly developed muscles, little subcutaneous fat, and undeveloped sexual organs. The heart may be enlarged, the cardiac impulse increased, the arteries strikingly narrow and tense; there is an absolute incapacity of undergoing even slight exertions, which defies treatment. The affection continues for years.

The heart frequently produces a split first sound, or even a systolic murmur. The increased strength toward the base of the heart, the absence of increase in strength of the second pulmonic sound, the venous murmur over the jugular veins when the head is in a forward position, are indicative of its functional nature. There are many theories about the origin of the abnormal cardiac sounds, but no positive explanation, whereas the venous murmur probably arises in connection with the

decreased specific gravity. Cardiac dulness is seldom enlarged, presumably owing to the retraction of the lungs; this is also said to be shown by X-ray examination. Œdema is not frequent in children. As mentioned already, the gastric complaints are mostly of a nervous nature, the secretion of acids is normal or more than normal, assimilation of food good (Lipman-Wulff). Menstruation is generally delayed and irregular, frequently painful. There is often a mucous discharge which stains the underclothing barely yellow. Occurrence of acne and urticaria is considered by many to be connected with chlorosis. The urine is normal or increased in quantity; when improvement takes place, there is said to be increased diuresis, according to von Noorden. The latter author, Eichhorst and Hayem also consider fever to be connected with chlorosis.

Among the complications ulcer of the stomach may occur even in quite young girls; thrombosis, however, ought to be rare in children. Advanced anæmia may favor the development of scoliosis in growing individuals.

Course and Prognosis.—Some cases of chlorosis take an acute course in otherwise well nourished and apparently healthy persons and are gradually cured under proper treatment in three to six months. This may be the signal for a permanent cure, but there may still lurk a tendency to relapses which are said to occur principally in the spring or late summer. Chlorosis which has commenced in early childhood may under favorable circumstances and proper care also be cured, but here a prognosis of a complete return to health is uncertain. It is just in these cases that in later years hypoplasia of the vascular system sometimes becomes manifest, or else there is a tendency to relapses and development of neurosis in more advanced age.

The **diagnosis** requires in the first place exclusion of all organic lesions especially on the part of the lungs, intestinal parasites or of ulcer of the stomach, which lead to secondary anæmia through hæmorrhages, and finally of renal affections. The diagnosis of chlorosis is supported by the age and sex of the patient, the history of the case and by the decrease of hæmoglobin, which is considerable in comparison to the decrease in red blood corpuscles. In pronounced changes of the blood (considerable poikilocytosis, normoblasts) the assumption of a secondary anæmia always suggests itself. The only question is whether cases where the blood changes are only slightly pronounced, but their manifestations are present, should be classed with chlorosis. In practice this has formerly always been done, and perhaps it is superfluous even now to carry through a distinct separation. The pathological picture is the same and perhaps the assumption is correct that blood changes are more in the nature of a symptom which occurs in female persons and then only at a certain age. For purposes of therapy, however, the examination of the blood is very important.

Prophylaxis commands a wide and grateful field in the prevention of chlorosis, because under proper care vicious tendencies undergo an improvement in the growing organism. The principal considerations are care for sufficient and correct nutrition, the correct distribution of work and recreation, sufficient stay in the open air, and abundant sleep. Further directions on this subject are given on page 137. It should be emphasized, however, again and again that the growing body should not be compressed into a narrow corset.

Therapy.—Medicinal therapy is of special importance when fairly marked blood changes have been demonstrated. The iron therapy, inaugurated in Germany, by von Niemeyer, has retained its advocates in spite of Bunge's adverse criticism.

Now, how does the iron take effect? The fact that even chlorotic patients obtain sufficient iron in the ordinary mixed diet is certain, because the organism contains 3 Gm. of iron, the feces contain 0.007–0.008 Gm., and Hoffmann estimated the daily total loss of iron at 0.06 Gm.; and this figure may still be too high. It follows that the cells of chlorotic patients do not assimilate sufficient quantities of the iron contained in the articles of nutrition in the shape of nucleo-albumin. What then is the effect of the inorganic iron? Formerly it was thought that it was not absorbed, from which originates the theory that it protects the organic iron from decomposition by combination with H_2S, and that it exercises a tonic effect upon the stomach. But the ferric nucleo-albumin of the food by no means undergoes ready decomposition, and, besides, iron introduced subcutaneously was supposed to have a beneficial effect. Recently the fact has been established (Müller) that also the organic iron compounds in medicinal doses can be absorbed and introduced into the organism by way of the general circulation. Indeed they served to increase the amount of iron in experiments on animals which had been deferrated by food containing but little iron; it was even an improvement on the iron contained in ordinary food. It is said that an increase of the nucleated red blood corpuscles in the bone marrow was demonstrated, which was regarded as showing an irritant effect upon the bone marrow. On the other hand, to supply with iron, cells which did not possess sufficient iron for constructive purposes is an entirely different matter from giving an additional iron salt to chlorotic persons whose bone marrow cannot assimilate a naturally sufficient quantity. At any rate, the iron therapy has obtained a secure foundation through the recent experiments, and it is probable that the irritant effect of the iron upon the blood-forming vessels, which had been assumed in theory to exist by Harnack and von Noorden, exists in fact. Possibly also the "fattening with iron" acts as an irritant.

What kind of iron preparation should be administered? There are two kinds to be considered: (1) those which are changed into oxide

salts by acids, including gastric hydrochloric acid, and into this category belong metallic iron, oxide salts, protoxide salts and ferric albuminates or peptonates; (2) compositions more highly constituted and more difficult to disintegrate.

Formerly it was said that the organic preparations are better absorbed and the building up of hæmoglobin in the organism is facilitated. The investigations above referred to, however, are in favor of inorganic or rather such iron preparations as are decomposable in the intestine. Grawitz reports having observed granular degeneration of the red blood corpuscles after the introduction of blood preparations.

Apprehensions as to the consequences of the iron therapy; blackening of the teeth, heaviness in the stomach and other gastric and intestinal disturbances, do not seem justified when sufficient caution is used. All iron preparations are to be taken on a full stomach with the exception of chalybeate waters which will be dealt with later; chalybeates and iron tinctures are administered through a glass tube and the mouth should be frequently cleansed and rinsed during the iron treatment on account of the iron deposit within the mouth. Should the feces assume a very black color, Henoch recommends to diminish the dose. Fats and acids, however, need not inspire apprehension. The treatment should last from 4 to 6 or 8 weeks, commencing and ending gradually; if necessary, the treatment is to be repeated after four weeks. As a rule, the daily dose for the adult is 0.1 Gm. (1½ grains) metallic iron in the preparations; children receive less in proportion. Character, percentage of iron and dose are shown in the following table according to Quincke and von Noorden:

Inorganic Iron Preparations and Simple Ferro-Albumin Compositions.

0.1 Gm. metallic iron is contained in:—	DOSE IN GRAMS
Ferrum hydrogenio reductum	0.1
Ferrum lacticum	0.5
Ferrum pyrophosph. c. ammon. citr.	0.55
Ferrum carb. saccharat.	1.0
Tr. ferri acet. aeth. (*Klaproth*)	2.6
Tr. ferri chlorat	2.8
Ferrum oxyd. saccharat solub.	3.6
Iron tropon	4.0
Iron somatose	5.0
Tr. ferri chlorati aether (*Bestuschef*)	10.0
Syr. ferri iodidi	11.0
Tr. ferri pomati	12.0–16.0
Liq. ferro-mangani sacch. u. pept. (*Helffenberg*)	16.6
Liq. ferri album	25.0
Malt extract with iron (*Löflund*, ferr. pyrophosph. c. ammon. citr. 2%)	27.5
Tr. ferri comp	50.0
Malt extract with iron (*Schering*, ferr. oxyd. sacch. solub. 3 %)	120.0
Pil. Blaudii (0.02 Fe)	5 pil.
Pil. aloët. ferrat. (0.03 Fe)	3–4 pil.

The tables show the frequently slight percentage of the higher-constituted iron compositions which often probably does not exceed that

of the blood (and therefore also of the blood sausage). The conditions, however, are favorable to resorption, and all these preparations have been successfully used. The table also shows the doses. Aside from the recipes mentioned on p. 139, older children may be given with advantage tr. ferri chlorati aether., three times daily 10–15 drops, and 1 or 2 Blaud's pills three times daily.

Iron Compositions not Readily Decomposable.

Composition.	Character.	Dose for adults.	0.1 Gm. inorganic iron is contained in.
Carniferrin	Composition of iron with carnophosphoric acid (Nucleon).	3 x 0.3–0.5	0.33 Gm.
Triferrin	Paranuclein and iron	3 x 0.3–0.5	0.45 "
Ferratin	Ferro-albumin from pig's liver	3 x 0.5–1.5	1.54 "
Spinoferrin			15.4 "
Hæmoglobin			23.3 "
Fersan		3 times 1 teaspoonful.	28.0 "
Hæmogallol	Blood-pigment reduced by pyrogallol	Twice to 3 times ½–1 teaspoonful.	35.9 "
Hæmol	Blood-pigment reduced by zinc	Twice to 3 times ½–1 teaspoonful.	38.1 "
Extract of Hæmoglobin (Pfeuffer)	Blood preparation, liquid		71.0 "
Hæmatogen (Hommel)	Blood preparation, liquid	3 times ½–1 tablespoonful.	142.0 "
Blood (human)			166.0 "
Sanguinal	Blood preparation, liquid	3 times ½–1 tablespoonful.	250.0 "
Hæmalbumin	Blood preparation, liquid	3 times ½–1 tablespoonful.	277.0 "

The subcutaneous injection (in the adult a 5 per cent. solution of ferrum citricum oxyd., 0.05–0.1 c.c. (♏ ¾–1½) into the nates; as recommended by Glaevecke, and Quincke) will hardly find application in the child; it causes smarting at the point of injection for 24 hours; rectal introduction (ferr. citr. oxyd. 0.1–0.6 c.c. (♏ 1½–9) in 50 c.c. (+ 1½ oz.) starch solution, three times daily, after Jolasse) is likewise hardly indicated.

Some excellent authors attribute a special influence to chalybeate waters (Henoch, von Noorden, Senator); their importance lies probably to a certain extent in the very high attenuation of the iron (0.01 to not more than 0.1:1000), also in the fact of their holding CO_2 in solution and in the possibility of administering the same on an empty stomach. If it is used at the springs, there are of course many other influences to be considered.

The saline carbonated waters are said to have the best effect probably on account of their purgative effect in constipation. Of the non-arsenious ones 1 pint is given (warmed, if desired) on an empty stomach in the morning, one pint and a half with the dinner, and the same quantity six hours after the principal meal. For home use pyrophosphorated iron water is more suitable because even with the greatest care in filling the bottles the iron is lost (Binz).

Should iron not have the desired effect, arsenic may be given to advantage, especially in weak-muscled children with enteroptosis. The doses are given on p. 140 and the admissible maximum dose is 1 mgm. ($\frac{1}{60}$ gr.) daily. Arsenious chalybeates are, of course, suitable in these cases.

Many physicians at the present time assist or replace iron medication by diaphoretic measures, prescribing a hot bath two or three times a week, followed by an hour's sweating, or else the use of the Phenix hot air apparatus (Grawitz, Rosin, Senator, Mamlock). Raebiger has made two series of experiments, one exclusively with iron medication and one exclusively with diaphoretics. The success of the second series was as large as that of the first. It is not certain, however, whether this is due to the water economy of the system or to the general effect upon the metabolism. Cold hydriatic measures should be avoided, the remarks made in regard to school anæmia (p. 135) applying to these cases likewise. On the other hand it is a very good plan to accustom the body to colder temperatures by the use of carbonic acid baths, of which 3 should be taken weekly (Senator and Frankenhäuser); also the effect of so-called mineral baths is probably based upon their containing CO_2, the iron they hold not being resorbed by the skin.

In regard to other dietetic methods, nutrition, good nursing, duration of sleep, gymnastic exercises (respiration), sport and games, the same remarks apply which were made in regard to school anæmia, also the remarks in regard to the treatment of complications. Chilblains are favorably influenced by long bathing of the extremities in hot water with a little alum, painting with ichthyol collodion (10 per cent.), inunction with camphoræ tritæ 5.0 c.c. (1 dr.) vaselini ad 50.0 c.c. (10 dr.). The discharge oozing from the vagina is hardly debilitating as is generally supposed; in these cases as well as in menstrual troubles, local treatment should be warned against (aspirin, antipyrin).

PERNICIOUS ANÆMIA

Nature, Etiology.—The name of Pernicious Anæmia designates an affection in which there is progressive diminution and degeneration of the red blood corpuscles, usually associated with fatty degeneration of internal organs.

Lebert (1852) and Addison (1855) had already described the pathological picture of severe anæmic conditions as a special kind of anæmia, and Biermer (1864) established its clinical lines of demarcation. The pathological anatomy of the bone marrow was described in detail by Cohnheim in 1878, while Ehrlich at a later period gave an exact description of the blood changes.

Formerly a distinction was made between pernicious anæmia with a known cause and a cryptogenic pernicious anæmia, but more recently some authors (Grawitz, Lazarus) are inclined to look upon the entire group as secondary disturbances, although there may be a difference in the congenital capacity of the blood-forming organs. The following causes have been observed: Chronic poisoning (carbon monoxide, Laache), tumors, especially of the bone marrow, infectious diseases

(sepsis, syphilis, malaria), bodily and mental injuries, disturbances of the digestive tract (autointoxications) and perhaps repeated small hæmorrhages. During pregnancy the affection is comparatively frequent. The best investigated kind is parasitic anæmia caused by bothriocephalus latus (Schaumann and Tallquist), anchylostoma duodenale (Zinn and Jacobi), also by ascarides lumbricoides (Demme). There is always a destruction of blood in this affection, as is evident from the large amount of iron contained in the internal organs, especially the liver, urobilinuria, manifestations of (nuclear) degeneration of the red blood corpuscles (Grawitz), but the bone marrow suffers secondarily an obstinate and perhaps permanent change of function. Ehrlich regards the change of the blood-forming function as anatomically characterized by the development of megaloblasts (especially large nucleated red blood corpuscles) in both bone marrow and blood; others do not consider this as specific, but only as an expression of the gravity of the anæmia.

Cases occurring in children have been described, but the affection is very rare in children. Many factors which are regarded as causative in the adult, enter rarely or not at all into consideration with children (pregnancy, psychic depression, tumors); it is also possible that the bone marrow of the child reacts differently.

Lazarus found among 240 reported cases 1 in the first decade (8 young girls by H. Müller) and 22 in the second decade. Then follow 11 cases compiled by Monti and Berggrün, 6 by Escherich, 2 by Grawitz (children of 12 and 8 years respectively), 3 by Koren, 1 by Theodor, 1 by Mott (a 9-months-old girl), 3 caused by anchylostoma by Baravallo, Villa, Cima. These few cases have not even been described with accuracy, some can hardly be accepted as true pernicious anæmia (Baginsky, 1 case by Retslag), others are doubtful (Senator). However that may be, a few certain cases have been observed even in the first year of life.

Symptoms.—The subjective complaints of children are: lassitude, weakness, headache, fainting spells, nausea, gastric pains, anorexia. Pains in the bones such as occur with adults in the tibia and sternum have not been mentioned in the case of children. Objective symptoms are the following: sallow complexion, fat cushion sometimes well preserved, frequently œdema of the legs, hæmorrhages in the skin of various extent, hæmorrhages in the mouth, also retinal hæmorrhages at an early stage; intestinal hæmorrhages have been observed comparatively frequently in children. The body temperature may be normal, in some cases however it is considerably raised, pulse frequent, respiration dyspnœic. The heart shows, aside from visible palpitation and pulsation of the carotids, sometimes enlargement to the left and right, and especially murmurs which may be diastolic and cause the distinct impression of cardiac insufficiency. Venous murmurs may be present. Diarrhœa

occurs frequently. Severe disturbances of consciousness also occur in children, but paralysis (from poisoning or anatomic changes) has not been observed. The spleen, usually enlarged in adults, is often swollen in children, but this may be the consequence of a complication. The urine in the adult is usually dark and often contains much indican (increased decomposition of albumin, Grawitz), also urobilin as a consequence of blood destruction. The oxygen consumption and the nitrogen metabolism, and also absorption, are frequently entirely undisturbed, provided there is light diet; Rosenquist in a bothriocephalus anæmia observed in the disease periods of increased decomposition of albumin alternating with normal conditions. The blood (Plate 8) is watery, of low specific gravity and considerably diminished coagulability. Hæmoglobin and red blood corpuscles are reduced to a minimum, and yet the coloring power of the individual corpuscle may at the same time be normal or even increased. This manifestation, however, can hardly be looked upon as specific. The white blood cells are relatively and absolutely reduced in numbers (although in one case of Grawitz 50,000 were counted in a child), the proportion to the red blood corpuscles in the adult is reduced to 1 : 1200 to 1600, and according to the majority of observations the lymphocytes have the highest percentage (up to 60 per cent.). The red blood cells do not exhibit any nummular formation, there is a strongly developed poikilocytosis, exceedingly small (dwarf corpuscles) and sometimes very large forms (megalocytes), further polychromatic and nuclear degeneration, associated with manifestations of regeneration (nuclear normoblasts and megaloblasts).

Anatomy.—Autopsy shows : enormous pallor of all internal organs, hæmorrhages, especially in the serous membranes, fatty degeneration, especially pronounced in the cardiac muscle, siderosis of the liver (hæmosiderosis), in some cases atrophy (anadenia) of the gastric and intestinal mucous membranes which however may not be regarded as a specific manifestation of the affection, transformation of the yellow marrow of the long tubular bones into red marrow, which may also occur in other anæmias (E. Neumann), whereas, on the other hand, yellow marrow may be found in pernicious anæmia (aplastic marrow, Ehrlich), in which case there should be no nuclear cells in the blood. The red marrow of pernicious anæmia is, according to Ehrlich, megaloblastic.

The **course** of the disease may be subacute or decidedly chronic, frequently there are also relapses following improvements. Death ensues in coma owing to progressive weakness.

The **prognosis** depends partly upon the cause. Can the latter be removed, as in the case of intestinal parasites, the affection is amenable to treatment. But also in the cases of obscure origin the prognosis is not absolutely unfavorable under appropriate therapy, a point again and again emphasized by Grawitz.

The **diagnosis** of pernicious anæmia is made by the hæmorrhages in the retina, possibly by a demonstration of urobilinuria, and finally by the blood examination. In children over four years old and in adults the demonstration of megaloblasts is important, but not in younger children. Against a diagnosis of pseudoleukæmic anæmia speak a diminution of the white blood cells, excessive diminution of the red, and perhaps a considerable poikilocytosis; on the other hand nuclear red cells exist in large numbers in pseudoleukæmic anæmia.

The **therapy** should pay particular attention to etiological conditions: the first thought should be of intestinal parasites; Lazarus' advice to administer an antiparasitic medicine (extract of male fern) even where no eggs can be detected, seems well worthy of consideration; the second thought is of syphilis (osteosclerosis), although the therapy (iodine and mercury) does not seem to hold out many chances in these cases; in the third place stand occult hæmorrhages especially in the gastro-intestinal canal—there are very exact methods of examination now to detect blood in the gastric contents and in the feces; in the fourth place should be mentioned the possibility of chronic effects of carbon monoxide and lead; in the fifth place, the gastro-intestinal canal should be treated by irrigation of the stomach and intestine, administration of hydrochloric acid, salol, calomel, or better by bitters, etc. The diet should be easily digestible, very nutritious (albuminoid with vegetables preponderating in the beginning). The appetite should be stimulated and care taken to provide rest, light and air. There is only one medicine which is sometimes attended with excellent results, and that is arsenic in drops or pills. Children of 8–15 years receive up to $\frac{1}{2}$–$\frac{3}{4}$ of the maximum adult dose; or it may be injected subcutaneously. According to Ziemssen's method 1 Gm. (15 grains) arsenic is dissolved in 5 c.c. (1 dr., ♏ 15) boiling normal soda solution, then distilled water is added to make 100 c.c. (3 oz., 2 dr.), and filtered; in adults a sterile injection is made of 0.001 c.c. (♏ $\frac{1}{60}$) up to 0.01–0.02 c c. (♏ $\frac{1}{6}$–$\frac{1}{3}$) daily; or sterilized subcutaneous injections may be made of sodium cacodylicum Merck in doses of 0.05–0.1 c.c. (♏ 1–1$\frac{1}{2}$) in adults. It is always necessary to commence with very small doses, increasing or diminishing the same slowly, this being the method to avoid intoxicating phenomena. Among the latter, pigmentation of the skin is without importance, while susceptibility of the buccal mucous membrane, gastric pains, diarrhœa, œdema of the eyelids, herpes zoster, would demand at least a temporary inhibition of the medication, although it is perfectly possible that these symptoms may partly be occasioned by the anæmia.

Finally the injection of small quantities of defibrinated blood in very grave cases should be considered. Surprising, although unfortunately only transitory results (Quincke, Ewald) have been attained by the introduction of small quantities (40 c.c.), the cause of which is prob-

ably to be found in the extreme reaction of the organism to its introduction (Bier), as shown by severe manifestations, high fever, etc.

LEUKÆMIA

Nature and Etiology.—Leukæmia is characterized by an excessive increase of the white blood-cells, swelling of the lymphatic and blood-forming vessels, and finally by the occurrence of lymphatic neoplasms in the organs.

Virchow was the first to correctly recognize the nature of the affection, demonstrating that there is an increase of leucocytes, whereas Bennet had thought of a kind of pus fermentation of the blood. Neumann particularly achieved considerable advance by his work on the blood-forming function of the bone marrow, while Ehrlich succeeded in perfectly differentiating the cells by proper staining methods.

Observations of leukæmia without anatomical findings are not quite safe (Hirschlaff), and Loewit's findings of amœbæ in leukæmic blood have not been confirmed by others. On the contrary, the majority of authors attribute leukæmia to a pathological condition of the blood-forming vessels. Formerly a distinction was made between leukæmia lymphatica and leukæmia lienalis, and when Neumann in 1866 discovered the fact that to the bone marrow belonged the function of forming the blood corpuscles, there was added a new kind: leukæmia medullaris. Later, in 1878, Neumann proved that in every case of leukæmia the bone marrow was involved, and therefore assumed (as did also Walz and Pappenheim) a myelogenous origin for all cases of leukæmia. On the other hand, Ehrlich and his disciples held that the lymphoid tissue is also to be considered as a source of origin, and therefore distinguishes between lymphatic leukæmia, caused by proliferation of lymphoid tissue (which, by the way, may according to Pincus have its principal seat not only in the lymphatic glands, but also in the lymphoid part of the medulla, the spleen or intestine) and myelogenous leukæmia, caused by proliferation of the typical medullary tissue. Clinically both forms are distinguished by the blood findings, which disclose in the first form principally lymphatic cells, and in the second granulated (medullary) cells. According to Ehrlich the difference is material, because the immobile cells of the first group can only be introduced into the blood by being passively swept away from the blood-forming organs, whereas in the second form there is active leucocytosis. According to some authors, however (especially Grawitz), the so-called lymphatic cells of lymphatic leukæmia are partly nothing but early stages of development of medullary cells (*i.e.*, really juvenile forms, as A. Fränkel expressed himself in opposition to Ehrlich). The lymphatic swellings of the organs are perhaps to be partly considered as new formations (metastases), in many cases however as hyperplasias of

pre-existing lymphatic foci. The question, however, whether the myeloid foci also originate through transformation of pre-existing lymphatic ones, is doubtful.

Following Ehrlich's initative the forms of leukæmia are now generally distinguished as lymphatic and myeloginous (myeloid, Pincus, mixed-celled, Pappenheim, Grawitz), according to the cells present in the blood. The former is usually acute, although there are also chronic cases; the latter mostly chronic although there are rare acute cases too (Hirschfeld, Alexander, Grawitz).

Etiology.—A parasitic etiology was supposed to exist, but not verified. The finding of a plasmodium by Loewit has not been confirmed by others. An infectious cause is probable in some cases according to A. Fränkel on account of the enlargement of the lymphatic glands of the neck in the first instance, and then by the subsequent course. But it is by no means certain that there is a uniform cause for leukæmia.

Bone tumors may likewise lead to a leukæmic blood picture, especially chloroma, which has derived its name from the green color of the tumors. The affection is most often found in children and young people. The seat of the new formation is preferably the periosteum of the cranial and trunk bones, but all the lymphatic organs may become involved. One of the earliest noticed symptoms is exophthalmos. Hæmorrhages and manifestations of rapid leukæmia supervene and the disease terminates fatally (Rosenblath, Risel).

As predisposing causes are considered syphilis, long-continued malaria, diphtheria, membranous angina, influenza, trauma; co-existing tuberculosis has also frequently been observed. Rare cases of infection and heredity have been reported.

Leukæmia generally attacks persons in the best years of life, but juvenile cases have likewise been observed. The male sex is chiefly attacked.

After Monti and Berggrün, Grawitz, Pinkus, and Lustgarten had reported cases in children, there have appeared more recent accounts by Bauer, Berghünz, Guinon and Jolly, Jeanselme and E. Weil, Kelly, E. Müller, Pollmann, Rocaz, Savory, Strauss, and Vermehren; a case of A. Fränkel was that of a boy. A few peculiar cases, the symptoms of which resembled those of pernicious anæmia, were described by Arneth-Leube, Geissler, Japha and Scharlau. Quite young children were affected in the cases of Pollmann, Strauss, Vermehren, in one by the author, and also in the cases of Bloch and Hirschfeld, Lehndorff, which are somewhat dubious as to classification. In the first four cases the number of leucocytes is so high (Japha 361,000) that the existence of a true leukæmia can hardly be doubted, difficult though the diagnosis in infants may be. Chronic myeloid were the cases of Berghünz (8-year-old girl) and Fleisch, a case from the Gratz Klinik (Pfaundler, 7

years) and the author's case, the course of which was somewhat subacute. As a rule, however, the acute lymphatic cases are the most frequent in childhood.

The *anatomical examination* discloses a more or less considerable swelling of the lymphatic glands, the spleen and the lymphoid follicles of the digestive tract. Besides, yellowish white foci may exist in all the other organs; the liver especially is usually considerably enlarged. The adipose marrow is of red color (lymphadenoid), but not corresponding to the normal red marrow, or of a deliquescent nature with cells of the medullary type. There are also hæmorrhages. The cellular foci in the organs consist of lymphoid cells, there is no necrosis. In the blood-forming organs the microscope reveals only a hyperplasia of the normally existing elements, but in lymphatic leukæmia the bone marrow consists almost exclusively of lymphatic cells, while in myelogenous leukæmia a myeloid degeneration of the spleen and lymphatic glands has been described.

Symptoms.—The affection commences suddenly or gradually with weakness, lassitude, anorexia, pains in the limbs or bones, especially in the left side (spleen). Mild or severe fever develops, the sallowness of the complexion increases, there is enlargement of the glands, spleen and liver, also hæmorrhagic diathesis. As the dropsical manifestations increase, death ensues, frequently caused by secondary septic involvements especially on the part of the tonsils, ulcerative stomatitis, hypostasis and pneumonia.

The blood is strikingly pale, clay-colored or milky. The determination of hæmoglobin is rendered difficult by the increase in white cells. In all cases there is an increase of the colorless cells up to several hundreds of thousands per c.mm., the proportion of the white to the red often being 1:20, less frequently 1:10 to 1:1. There is a considerable increase of mononuclear cells of the lymphatic type (see Plate 8, Fig. 5), which however may be of varying size, and especially in the acute form often attains to a considerable size (large lymphocytes, Ehrlich, medullary cells of several authors, not to be confounded with Ehrlich's granulated myelocytes; central germ cells, Benda); sometimes they are exceedingly friable. Polynuclear cells in these cases amount only to a few per cent. Often there is nuclear segmentation. In myelogenous leukæmia (mixed celled, see Plate 8, Fig. 4) there are aside from considerable augmentation of the polynuclear cells:

1. Mononuclear, neutrophile or eosinophile cells (Ehrlich's myelocytes) which do not exist in normal blood.

2. Absolute and relative augmentation of the "mastzellen" (polynuclear cells with basophile granulation).

3. Atypical cell forms (karyokinesis, extremely small or large forms, polynuclear cells with granulation slight or absent).

The red blood corpuscles are nearly always decreased, perhaps to 2 or 3 millions, and seldom are the values below. Nummular formation is nearly always absent, there are polychromatic and granular degenerations, nucleated cells (mostly normoblasts), less often poikilocytes, microcytes and megalocytes. In myelogenous leukæmia there are mast cells also in the exudates.

The glands, which are nearly always palpable, do not as a rule exceed the size of a hazel-nut, although at autopsy more extensive enlargements are often disclosed than were at first supposed. Also the other lymphatic formations, especially in the fauces, are œdematous, and here there are frequent ulcerations with consequent hæmorrhages and septic conditions, often there is an ulcerous stomatitis. The spleen is likewise œdematous, but does not usually attain to a very considerable size except in chronic leukæmia. The liver is often enlarged. Hæmorrhages which often defy control are visible in the skin and mucous membranes. The exudates are usually of a sanguineous coloration. Retinal hæmorrhages are hardly ever absent in acute leukæmia, sometimes there is a leukæmic retinitis with white foci. It is quite usual that very large quantities of uric acid are excreted with the urine (Virchow, A. Fränkel, Magnus-Levy).

The **course** may be very acute (death after 3 weeks), but many cases drag on for many ($4\frac{1}{2}$) years. In these cases there are temporary periods of improvement in the blood and general conditions. Septic infections may lead to a disappearance of the leukæmic blood picture and decrease of the swellings through a destruction of the cells, according to A. Fränkel (aleukæmic stage).

The **diagnosis** is based upon (1) the blood findings (very high polynuclear leucocytosis alone proves nothing); (2) enlargement of the organs; (3) hæmorrhagic diathesis (retinal hæmorrhages). In atypical cases the differential diagnosis may be very difficult as against pernicious anæmia (Geissler and Japha, Arneth-Leube). The difficulties in young children where there is already a relative lymphocytosis, and where there are also myelocytes, have already been dealt with (p. 160).

Therapy.—Operative interference (extirpation of lymph-nodes and spleen) has only an injurious effect. In view of the peculiar effect of infectious diseases upon the blood picture, remedies have been administered for their chemotactic effect (extract of spleen, spermin, tuberculin, nuclein, cinnamic acid), but all without success. Temporary success may follow after iron, arsenic, iodine, the latter being also used externally; quinine and phosphorus have been less successful. Attempts have been made to influence the spleen by ergotin injections, the application of the icebag, also in adults by berberinum sulf., three times daily 0.01–0.03 Gm. ($\frac{1}{6}$–$\frac{1}{2}$ gr.), dyspnœa by inhalations of oxygen. More recently the X-ray treatment has attracted attention in chronic cases which

were not yet complicated by grave anæmia. Considerable improvement has thereby been achieved and, although only in very few cases, also maintained for several years after discontinuance of treatment. The variation in success is perhaps explained to a certain extent by the treatment which varied according to site (spleen, bones, glands, liver) and the duration of exposure (daily or weekly, or a totality varying be-

Fig. 24.

Chronic leukæmia. Boy from Fig. 23. Anterior view of spleen.

Fig. 25.

Chronic leukæmia. Lateral view of spleen. Liver not materially enlarged.

tween fifty and sixty thousand minutes). The undeniable effect is explained by most authors (de la Camp) by the specific influence of the X-ray on the lymphoid tissue, by Arneth by their influence on the circulating blood (the supposed micro-organisms).

PSEUDOLEUKÆMIA

Nature, Name and Forms.—Pseudoleukæmia simulates leukæmia by its clinical course, the appearance of the patient, and the anatomical

findings (hyperplasia of all lymphatic formations), although the principal sign, the "white blood corpuscles," is missing. The name given to this affection by Cohnheim in 1865 chiefly expresses something negative, and similarly the various other names under which similar symptom complexes are grouped (adénie, Trousseau; lymphosarcoma, Virchow, Langhans; malignant lymphoma, Billroth; lymphatic or splenic anæmia, Griesinger, Strümpell) mark the uncertainty of the clinical picture. The designation of Hodgkin's disease is explained by the fact that Hodgkin in 1832 published observations on hyperplasia of glands and spleen which produced general manifestations; leukæmia as such was not yet discovered at that time and his observations therefore hardly referred to a uniform affection.

Like leukæmia, pseudoleukæmia was also formerly differentiated as pseudoleukæmia lymphatica and lienalis, according to the chief enlargement, to which was added pseudoleukæmia medullaris later on, but according to more recent investigations the primary origination from the glands is decidedly the most frequent; exclusive localization in the spleen is rare, while an affection of the medulla leads in most instances to leukæmia (Neumann, Grawitz). Pappenheim is of the opinion that the same irritation produces pseudoleukæmia and leukæmia according to whether it affects only the lymphatic glands and spleen or also the medulla; similarly Pincus places the affection in close relation to leukæmia, principally based upon a relative lymphocytosis which he has always found in true pseudoleukæmia. Grawitz, on the other hand, was unable to verify this observation by the material at his disposal. After some previous investigators (Askanazi, Weishaupt, Brentano and Tangl) had discovered tubercle bacilli in pseudoleukæmic swellings, C. Sternberg published the remarkable fact that 15 out of 18 closely observed clinical cases were founded on tuberculosis, in which the microscope revealed a difference from true lymphomata by the existence of special cells and caseation, without the necessity of the presence of the typical blood picture. While admitting that tubercle bacilli may be found accidentally in pseudoleukæmic glands, yet the great frequency of the findings justifies the conclusion that the major part of the observed cases of pseudoleukæmia are attributable to a tuberculous affection of the lymphatic structures (also in animal experiments tuberculosis may cause lymphomata of simple appearance). Grawitz, however, states that a difference between these cases and true pseudoleukæmia can not be clinically established, that both groups may be equally influenced by arsenic and he thus makes the etiology the basis of a classification by differentiating pseudoleukæmias of a simple lymphomatous (better perhaps "lymphomatosis of unknown origin"), tuberculous and syphilitic origin. The common symptom is the clinical picture: the progressive involvement of all the lymphatic organs. According to many observa-

tions formation of lymphomata follows in the wake of an inflammatory process in the root area of the lymphatic glands (gastric affections, chronic coryza, defective teeth, inflammations of the ear), supposedly also of malaria, whooping-cough, dysentery. Reported cases of family affections do not stand criticism.

Occurrence.—Youthful individuals are chiefly affected, and the period of childhood is considerably involved. Fischer had 7 children among 12 patients, Meyer among 76 cases, 11 up to 10 years and 7 up to 20 years of age; Falkenthal out of 40 cases 8 in the first and 11 in the second decade. It is not known in how far the tuberculous form prevails.

Anatomy.—At autopsy an extensive involvement of the lymphatic system, also foci in the internal organs, are disclosed as in leukæmia, but often still more extensive than in the latter. The simple lymphomata behave under the microscope precisely as those of lymphatic leukæmia. In the cases of tuberculous involvement Sternberg found singularly large mononuclear or polynuclear cells with abundant protoplasm and large nuclei, often with nucleated corpuscles, also karyokinesis. Frequently there are necrotic foci which do not occur in true lymphoma; tubercle bacilli and typical tuberculous tissue are not seen in all cases. The medulla has not frequently been included in the field of examination. More frequently amyloid degeneration has been observed, sometimes also true tuberculous affections of internal organs (Fischer).

Symptoms and Course.—The course is such that a group of lymphatic glands, most frequently cervical, swell on one or both sides of the neck, growing to lobular tumors sometimes of a larger size than the fist of a man. Sometimes the lymphatic structures of fauces, tongue and tonsils are involved from the first. Then proliferation begins in a neighboring glandular group or on the opposite side. One gland after another, corresponding to the lymphatic current, is involved in the proliferation, until the new formation reaches into the cavities of the body. Then there are metastases in the remote glands, in the internal organs, followed by enlargement of liver and spleen. The spleen may reach an enormous size; sometimes there is tenderness in the bones. The numerous swellings frequently lead to manifestations of compression, pressure in the vessels leads to engorgement in the upper or lower half of the body, pressure on the trachea and œsophagus causes difficulty in respiration and swallowing. Finally cachexia and anæmia develop. The blood shows a diminution of hæmoglobin and red blood corpuscles, but grave changes in the erythrocytes are less frequent. The white cells are often moderately increased. An increase of lymphocytes (Pincus) only occurs in simple lymphomata, but according to Grawitz is not always present, while in cases with a tuberculous foundation there is usually polynuclear leucocytosis. The skin is more frequently involved, there are pruritic affections, subcutaneous lymphomata, also purpura. The

urine, on the whole, does not present any definitely established peculiarities; sometimes there is albumin, especially when there is amyloid degeneration which occurs rather frequently. Fever is one of the usual manifestations and may be very high. Ebstein thinks he can establish a special type as that of chronic relapsing fever, in which febrile and afebrile periods alternate.

The **duration** of the affection may occupy years, exacerbations may alternate with improvements of the general condition and reduction of

FIG. 26.

Pseudoleukæmia. Six-year-old boy with hard, lobular, glandular tumor, the size of a child's head a smaller glandular tumor in the axilla. Distinct manifestations of engorgement in the left half of the face. The glandular tumor of the neck will be extripated. There are glands without caseation and true tuberculous changes. Final outcome uncertain.

the glands; intercurrent diseases (varicella, measles) sometimes effect a transitory improvement (Bendix). In the end death usually ensues from cachexia, amyloid degeneration, septic affections, or pneumonia.

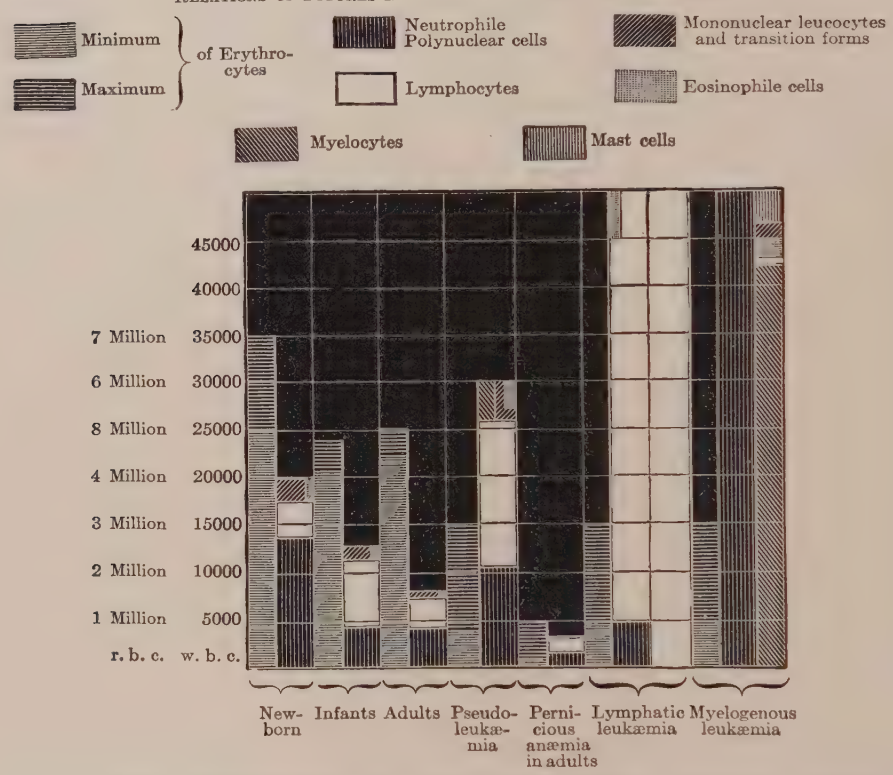
The **prognosis** is always doubtful, and although a cure is not absolutely excluded (Katzenstein, Grawitz), relapses may at any time be expected. In some cases the therapy may be able to postpone the unfavorable termination for years.

The **diagnosis** cannot be established with certainty at the onset of the disease; later this is easier. Scrofulosis generally does not produce glandular enlargements of such magnitude; in pseudoleukæmia, too, the other scrofulous symptoms are absent, such as blepharitis, coryza, phlyctænular affections of the cornea, aural secretions. Lymphoma on a tuberculous

foundation (Sternberg) may be distinguished from a simple lymphoma at autopsy only. Differentiation from leukæmia is only possible by the examination of the blood. There is a peculiar difficulty in the first stage of the disease by the presence of lymphosarcomatous affections (Kundrat). At first they commence precisely like pseudoleukæmic swellings, but then they break through the glandular capsules and lead to adhesions of the glands between each other and their surroundings;

FIG. 27.

RELATIONS OF FIGURES IN NORMAL AND PATHOLOGICAL BLOOD



The left columns, hatched transversely, give the minimum and maximum of the red blood corpuscles, the right ones give the proportion of the colorless corpuscles. For instance the diagram shows at once the large number of lymphatic cells in pseudoleukæmic anæmia and their almost total disappearance in myeloid leukæmia.

besides, ulcerations of the buccal mucous membrane and the upper air tracts may develop. The recognition of solitary splenic enlargements is often difficult.

In regard to **prophylaxis** some authors recommend the extirpation of glandular enlargements of long standing which resist other treatment. Otherwise the remarks made for leukæmia apply here likewise, including operative therapy and X-ray treatment which—at least temporarily—may without doubt have a favorable influence on the enlargements

and the general conditions. The only point to be added is that intelligent treatment with arsenic is attended with undeniable success, if applied in accordance with the maxims laid down on p. 139. Even complete recoveries have been reported which had not too far advanced (Grawitz, Katzenstein).

AFFECTIONS OF THE SPLEEN

The spleen becomes enlarged in many infectious diseases, as in typhoid, paralysis of recurrent laryngeal nerves, malaria, tuberculous meningitis, parotitis. Considerable enlargements occur in leukæmia, pseudoleukæmia, and brief mention may be made of echinococcus of the spleen.

Of rather frequent occurrence is anomaly of position, *splenic ptosis.* It is found even in infants and is nearly always associated with a general flabbiness of the entire musculature, especially that of the abdomen, often also with a diastasis of the recti muscles. In older children there is usually a general enteroptosis including the downward displacement of liver and kidneys. Generally these children are languid, of marked nervous irritability and small appetite. In these cases the complaints depend not so much on the displacement as on the nerves, and only occasionally has a disturbance originating with the spleen (kinking of the intestine) been observed in adults. The diagnosis is established from the general condition; again, the prolapsed spleen is much softer than one really enlarged. The therapy endeavors to improve the nervous complaints, the general circulation, to effect a slight fattening, and is therefore to follow the same directions as in infantile anæmia where a similar enteroptosis is occasionally observed.

The so-called rachitic enlargement of the spleen is not a typical accompaniment of rachitis, as has been stated by Henoch. Sasuchin found splenic enlargement 12 times in 66 cases, Geissler and Japha 22 times in 75, Cohn only 58 times in 858 cases. Sometimes it is only simulated by prolapse with engorgement, and for this reason a spleen which was distinctly palpable during life, is sometimes not found enlarged at autopsy. Real enlargement, however, may sometimes have a connection with a coexisting anæmia. Enlargement of the spleen is probably not caused by rachitis, but at the most by a factor similar to the one which caused the latter.

Syphilitic splenic enlargement sometimes occurs quite independently. In congenitally syphilitic infants it is not found so frequently as is sometimes stated. On the other hand there are sometimes very considerable enlargements in older children with congenital syphilis, although recent syphilitic manifestations need not be present. Sometimes the diagnosis can be established only from the history, in other

cases the condition is indicated by infantilism and Hutchinson's teeth. Usually there is also an enlargement of the liver, in rare cases syphilis of bones and joints. These manifestations are difficult to treat even by energetic antisyphilitic therapy.

The so-called Banti's disease (anæmia accompanied by splenomegaly) begins, according to this author's description, with enlargement of the spleen which, in conjunction with anæmia, may in the course of years assume considerable proportions. The anæmic stage having lasted for several years is complicated by ascites and hepatic cirrhosis, and the patient dies from hæmorrhages under dropsical manifestations (Senator). The blood findings are characterized by considerable oligochromæmia, then oligocythæmia, also leukopenia, with a preponderance of lymphocytes. Banti attributes the affection to an intoxicating process emanating from the spleen, and indeed some authors (Maragliano, Bessel-Hagen) report having effected cures by extirpating the spleen. The affection has often been observed in children (Osler 11-year-old girl, Morse 7-year-old boy, Senator 15-year-old boy, Pribram 15-year-old boy). The diagnosis can only be established after exclusion of all other causes of enlarged spleen. The only cure is held to be the extirpation of the spleen, while leukæmia is not influenced by this operation. Latterly, Chiari, Marchand, looked to late hereditary syphilis for the cause of similar cases, because a distinct lobulated liver was discovered at autopsy. According to this finding the liver must be at least involved simultaneously with the spleen, and the extirpation of the spleen would simply act like Talma's operation on the existing ascites. If these reports should be verified for at least part of the cases, the therapy ought to be antisyphilitic; the effect, however, can only be conditional, because the pathological process has already partly run its course by the time it comes under observation.

AFFECTIONS OF THE BONE MARROW

Red marrow fills the medullary spaces of the short and flat bones (sternum, ribs, vertebræ, cranial bones) and also the diaphyses of the long tubular bones in the fœtus. Soon after birth the red marrow begins to be replaced by adipose marrow, the transformation being complete in the diaphyses of the tubular bones. The red marrow, however, soon returns when an irritation is exercised by certain diseases (infections) or hæmorrhages. The "red marrow" of pernicious anæmia differs from the normal red marrow; according to Ehrlich it is megaloblastic, and the leukæmic marrow, too, deviates from the normal. Latterly the bone marrow has been credited the rôle of storing up protective substances in infectious diseases.

In adults a tumefaction has several times been observed in the

medulla, the so-called myeloma (Mahler, Senator). It consists of lymphoid cells or cells of the medullary type. It chiefly affects the ribs and short bones, later also all the other bones. As a sequel grave anæmia occurs of the pernicious type. The urine contains Bence-Jones' albuminoid bodies. No cases have thus far been observed in children.

SYMPTOMATIC ENLARGEMENT OF THE SPLEEN

The spleen is enlarged in many infectious diseases, as for example in typhoid, malaria, tuberculous meningitis, and parotitis. Enlarged spleens are present in leukæmia, pseudoleukæmia and also in ecchinococcus of the spleen.

Ptosis of the spleen is an anomaly of position of rather frequent occurrence. It is found in nursing infants and is almost invariably associated with a general relaxation of the musculature, especially the abdominal muscles. A diastasis of the recti muscles is quite frequently present. A general enteroptosis is usually found in older children, associated with ptosis of the liver and kidneys.

These children as a rule are easily fatigued, show nervous irritability and poor appetite. The symptoms depend more on their nervous condition than on the ptosis. This disturbance among adults is seen only occasionally, depending on this condition of the spleen (twisting of intestines).

The **diagnosis** is made on the general condition. The spleen in ptosis is found to be softer than in a really enlarged spleen.

The **treatment** should be directed toward the improvement of the nervous condition, circulation of the blood, forced feeding, etc., as in anæmia of children, among whom this condition of enteroptosis is occasionally seen. Arsenic is of special value.

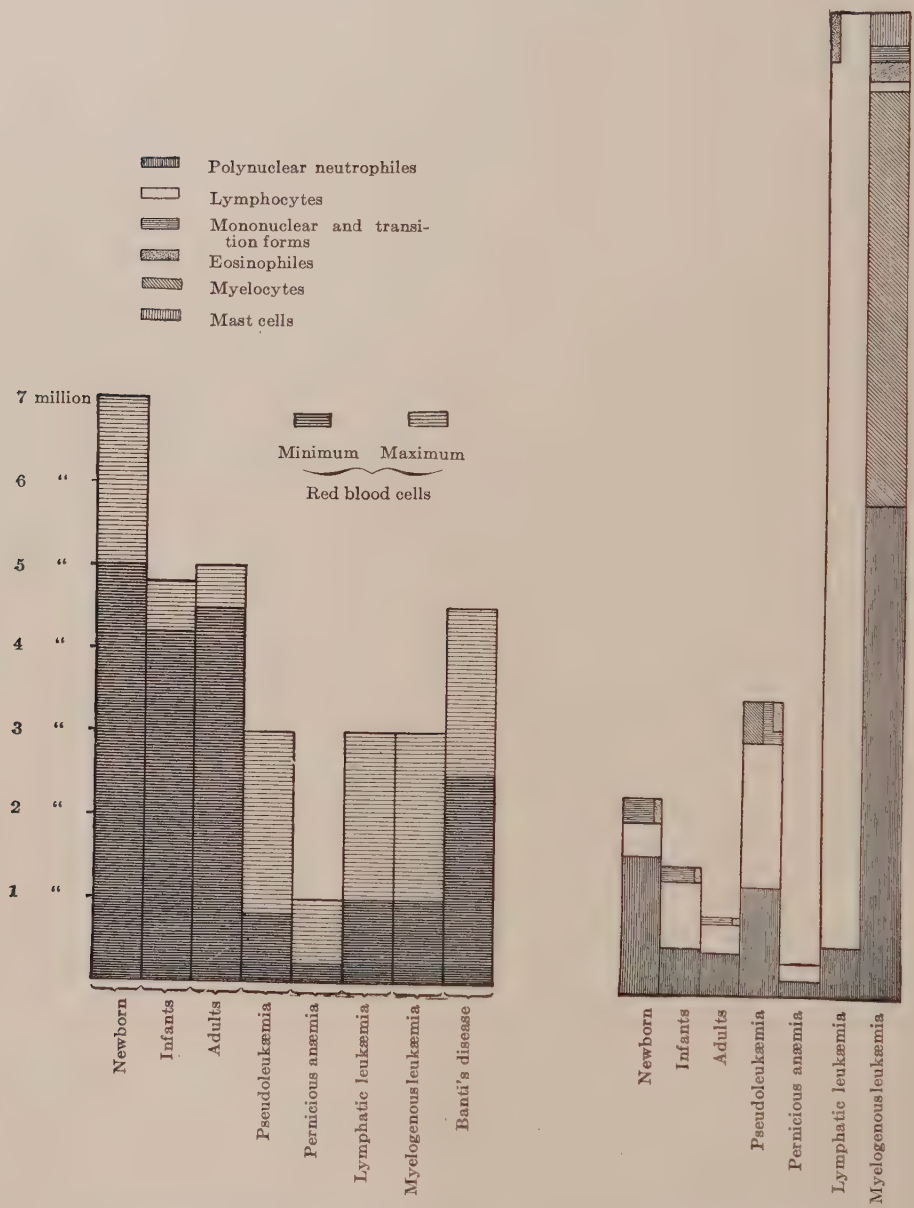
The so-called **rachitic spleen tumor** is not a typical concomitant symptom of rachitis, as pointed out by Henoch. Lasuchin found enlarged spleen present in 12 cases among 66, Geissler and Japha in 22 cases among 75, Cohn of 858 cases in only 58 cases. At times a ptosis of the spleen with resulting congestion resembles an enlarged spleen when on autopsy the spleen is not found enlarged but which during life was distinctly palpable. A real spleen tumor, however, may occur in connection with anæmia. It is certain that splenic enlargement is not caused by rachitis, but is rather secondary to a similar pathological process.

Syphilitic spleen tumor sometimes appears quite independently. In young children with congenital syphilis it does not occur nearly as frequently as is stated. But very large spleen tumors are seen in older children with congenital syphilis even when no recent syphilitic symptoms are present.

The **diagnosis** may depend only on the history; in some cases it may be made from the greatly weakened physical condition, Hutchin-

son's teeth, and in doubtful cases from a positive Wassermann reaction. As a rule there is associated with it an enlargement of the liver and in

FIG. 28.



Red blood cells in normal blood and in diseases of the blood.

White blood cells in normal blood and in diseases of the blood.

rare cases severe bone- and joint-syphilis. These lesions do not yield readily to the most energetic antisyphilitic treatment.

There is a disease, endemic in India and occasionally occurring in Russia, which is characterized by anæmia, swelling of liver and spleen, called *kala-azar*. Fever is present but no icterus. Cachexia is marked as the disease approaches a fatal termination. Aspiration of the spleen yields a fluid containing Leishman's bodies, stained after the method of Giemsa-Romanowski. Bedbugs are believed to be the carriers of the disease. Among those afflicted are many children. Sluka and Zarfl reported a case of a Russian child coming from Russia, so it is well, therefore, to keep this disease in mind.

MORBUS BANTI

Clinical Picture.—The disease begins, according to Banti's description, with a spleen tumor accompanied by anæmia, the tumor becoming quite large in the course of years. After a duration of 3 to 10 years the anæmic stage is followed by a transitional stage with icterus and gastro-intestinal disturbances lasting several months; later ascites and cirrhosis of the liver develop, with an occasional rise of temperature in some cases, and there are œdema and hæmorrhages as the disease reaches a fatal termination.

Examination of the *blood* shows marked oligochromæmia, aligocytheæmia, also leukopenia, the lymphocytes being increased; the increase of lymphocytes however is not always marked, not even in the case of Caro verified by operation.

Occurrence.—The disease has frequently been found among children (Osler, eleven-year-old girl, Morse, seven-year-old boy, Senator, fifteen-year-old boy, also Pribram, Dose and Finkelstein).

Pathology.—There is marked sclerosis of the splenic vessels (also endophlebitis of the splenic veins), sclerosis of the portal vein, change in the stroma of the spleen with formation of new connective tissue and principally with fibrous degeneration and destruction of the spleen follicles; later an interlobular atrophic cirrhosis of the liver develops, which, however, is never very marked.

Banti believes that the disease is a toxæmia originating in the spleen, demonstrated by the fact that extirpation of the spleen has undoubtedly been followed by marked improvement. It has been observed that certain material and body substances as spleen cells may reach the liver by way of the splenic veins. Those who regard the disease as a toxæmia originating in the gastro-intestinal tract may base their opinion on Caro's finding of an achylia gastrica in his case. It seems, however, that many cases of quite a different nature are classed with this disease only because of a certain remote similarity. In a case of Eden, a thrombus of the portal vein was the cause, in a case of Hedenin there was found on autopsy a stenosis of the "valvula Bauhini" and the disease no doubt developed from a spreading of the inflammation to the portal vessels.

The recognition of the disease is rather difficult. One case, greatly improved after operation, showed syphilis of the liver two years later on autopsy. Chiari and Marchand had to diagnose syphilis in some cases resembling typical morbus Banti, because of syphilitic scars found on autopsy. Many pathologic anatomists regard the disease as identical with cirrhosis of the liver and point out the fact that precirrhotic spleen tumors do occur, as well as a greatly enlarged spleen in connection with cirrhosis of the liver. On the other hand, Bleichroeder is of the opinion that cirrhosis of the liver has its origin in the portal vein and should be classed with diseases of the blood. Although not all these conclusions can be accepted, it is nevertheless possible that the same toxin on the one hand attacks the blood and blood-forming organs, on the other hand the liver, and the favorable result following extirpation of the spleen is not sufficient proof that the origin of the disease is in the spleen.

A positive **diagnosis** can be made only after all other causes of spleen tumor can be excluded, as for example chronic leukæmia and lymphosarcoma of the spleen. According to above facts, the differentiation from liver cirrhosis (especially on a syphilitic basis) is rather difficult or even impossible. The primary large spleen tumor and the blood picture above described speak for Banti's disease, as well as the pathological finding, which in case of morbus Banti is an indurated, in case of cirrhosis of the liver a soft, spleen.

Treatment.—Extirpation of the spleen has many advocates. According to Banti the spleen is the cause of the disease, while others believe this operation beneficial only because of its effect on the existing ascites. The result in some cases is certainly gratifying, as shown by the cases following splenectomy reported by Maragliano, Bessel, Hagen, Armstrong, and Caro. The case of Caro, which was carefully observed, proves that even the anæmia disappears after operation. The operation, however, is not without danger. Shiassi has, therefore, advised a splenocleisis. Owing to the limited material we do not know the duration of the beneficial results of the operation. The course of the disease extends over a number of years even without operation. The writer has under observation a case of morbus Banti in a man who had an enlarged spleen eight and a half years ago, and the first attack of hæmatemesis five years ago, also a case in a boy of sixteen years for five and one-half years. As in the majority of the cases syphilis seems to be the etiological factor, a trial of antisyphilitic treatment would appear rational, although the results are limited because the process has, as a rule, run its course when the disease comes under observation. Hering reports one case where X-ray treatment was followed by good results after an attempt at operation proved fruitless because of adhesions. The writer can not report success with X-ray treatment in his cases. Continuous sun-baths (the body was exposed to the direct rays) resulted in marked improvement in a case

	Hæmoglobin	Red blood cells	Hæmoglobin index	White blood cells
Blood of newborn	100–140%	5–7 millions	.....	20,000 and over
Blood of infants	85–114%	4.1–4.8 millions	.....	12,000 to 13,000
Blood of adults	100%	4.5–5 millions	.....	8000
Post-hæmorrhagic anæmia	Greatly diminished	Greatly diminished. Poikilocytosis and microcytes. Rarely nucleated cells and normoblasts	Diminished during regeneration	Polynuclear leucocytosis during regeneration
Chlorosis	Greatly diminished	5 million to below 1½ millions. Swelling of the cells increases the size	Extremely low	Normal
Pernicious anæmia	Diminished	As low as 200,000. Difference in size and shape of cells. Normoblasts, megaloblasts	Increased	Leukopenia with relative lymphocytosis
Severe infantile anæmia (pseudo-leukæmia).	Much diminished	As low as 800,000; large number of normoblasts, megaloblasts. Marked polychromasia. Moderate poikilocytosis	Increased or diminished	Increased to 50,000
Acute lymphatic leukæmia	Diminished	Diminished to 1 million. Variable blood picture	Increased in severe anæmia	Increased to 100,000 and over
Chronic lymphatic leukæmia	Diminished	Diminished to 1 million	Normal, occasionally increased	Increased to 100,000 and over
Pseudoleukæmia: (*a*) Real pseudoleukæmia	Diminished	Diminished, often severe anæmic changes	.....	5000 to 10,000
(*b*) Granulomatose	Diminished	Diminished, often severe anæmic changes	.....	Increased to 50,000
(*c*) Lymphosarcoma	Diminished	Diminished, often severe anæmic changes	.....	Often increased
Banti's disease	Diminished	Diminished	.....	Diminished
Chronic acholuric icterus	Diminished	Diminished, often normoblasts and megaloblasts	.....	Slightly diminished

eosinophiles	Large mononuclear cells and transition forms	Lymphocytes	Mononuclear neutrophiles	Mononuclear eosinophiles	Mast cells	Clinical picture	Anatomical findings.
	8%	20%	P	resen	t		
%	8–10%	50–55%	P	resen	t in		
	4%	34%	first Occa	week sional	s ly		
			p	resen	t		
						Spontaneous anæmia without apparent cause and with the blood picture occurring in girls at the time of puberty. Naegeli considers a great desire for sleep characteristic	
ne d		Increased to 60%	41	–2%		Extreme anæmia, gastro-intestinal symptoms, cardiac murmurs and retinal hæmorrhages. Achylica gastrica with increased mortality. Urobilinuria	Fatty degeneration of the inner organs (heart muscle), hæmosiderosis in liver, spleen, kidneys, etc.
	2%	52%	5%	1%	0.5%	Anæmia with petechia. Enlarged spleen, slightly enlarged liver	Decrease in granular elements in red bone marrow. Hæmorrhages in liver, spleen, and glands. No development of follicles in spleen and glands. Hæmosiderosis.
		Increased to 90%. Differences in size and shape	Occa	sional	ly	Enlargement of lymphatic glands, spleen and liver. Fever. Hæmorrhagic diathesis, gangrenous processes in intestinal tract. Uric acid in excess, retinitis, lymphomata of skin, septic diseases, rapid course	General affection of lymphatic tissue. Lymphomata in all organs. Bone marrow dark red. The small cell forms described by Naegeli often grown through capsule of gland.
			pr	esent	in		
			ea	rly st	age		
	1%	1%	41	%	3.5%	Often commences with abdominal distention and pain around spleen. Slight fever. Slight involvement of lymphatic glands. Enormous spleen. Death from cachexia or intercurrent diseases. Slow course	General affection of myeloid tissues. Myeloid degeneration of liver and spleen. Charcot-Leyden crystals in blood.
		Up to 90%				Course and clinical picture similar to leukæmia. Hæmorrhages, no fever. Benefited by arsenic and X-ray. Rare in children	General affection of lymphatic glansd with formation of foci in lymphatic tissues. No regressive metamorphosis.
		Diminished	Of	ten		Tumors of lymphatic glands (mediastinum), enlarged liver and spleen. No affection of mucous membranes, no hæmorrhages. Diazo-reaction. No benefit from arsenic and X-ray. More frequent and of rapid course in children	Characteristic affection of lymphatic system with formation of granulation tissue with many epithelioid cells, eosinophiles. No round cells. Tendency to regressive metamorphosis. Cause tuberculosis or syphilis.
			pre	sent			
		2–27%				Begins chiefly in glands of neck, mediastinum, spleen. Compression symptoms, thrombosis, rarely fever. Benefit from arsenic and X-ray.	Local disease of lymphatic glands at first, progresses into lymph channels. No metastasis in blood vessels.
		Increased				Anæmia and enlarged spleen of long duration. Later ascites and cirrhosis of liver	Sclerosis of blood vessels of spleen and fibrous hardening of spleen follicles. Later atrophic cirrhosis of liver.
		Diminished	Occa	siona	lly	Often hereditary, characterized by chronic icterus, urobilinuria, cholic stools, enlarged spleen and liver. Chronic course	
			pre	sent			

already suffering from serious circulatory disturbances; the improvement has lasted for years. It is possible that there is a development of vessels between the spleen and the abdominal wall.

SPLENOMEGALY OF GAUCHER, AND CHRONIC ACHOLURIC ICTERUS WITH OR WITHOUT ENLARGED SPLEEN

In addition to morbus Banti there have been quite recently two new diseases of the blood described, which are perhaps identical, as they certainly strongly resemble each other as well as morbus Banti.

I. Splenomegaly is characterized by an enlarged spleen, lasting for years (up to 39 years!), often congenital, associated with enlarged liver, anæmia, but never with ascites, and often with a brown pigmentation of the skin. The disease is frequently found to be hereditary. The examination of the blood shows nucleated erythrocytes, also megaloblasts, the color index is increased and the blood picture of the white corpuscles was found to vary. Anatomically groups of endothelial-like cells are found in the spleen, liver, lymph-glands and in the bone marrow. It is, therefore, a systemic disease (Schlagenhaufer). Not infrequently tuberculosis is associated with the disease.

II. Another disease, known as **chronic acholuric icterus,** is characterized by chronic icterus, urobilinuria and enlargement of the spleen. The latter symptom is not always present. Frequently the liver is enlarged and changes in the blood take place in certain cases, such as a diminution of the red corpuscles, presence of nucleated red cells, also megaloblasts, slight leukæmia with neutrophilic cells predominating, also myelocytes. The blood serum is icteric, the urine free from biliary coloring matter, but it does contain urobilin and urobilinogen. The stools are choleric. The affection is chronic, causing but slight constitutional disturbances, and there appears to be a family predisposition to the disease.

French authors associate the symptom-complex with a disease of the liver, but German authors on the other hand, among them Benjamin and Sluka, believe it to be an affection of the hæmatopoietic system. In their opinion there is an association of the systemic disease with an increased destruction of blood elements, characterized by marked siderosis in the organs and perhaps by increased excretion of uric acid. They regard icterus as the consequence of the destruction of erythrocytes.

We would again refer to the statements of Bleichroeder mentioned in connection with morbus Banti. In cirrhosis of the liver similar changes have been observed in the gastric mucous membrane as in diseases of the blood, such as a marked deposit of ferruginous pigments and many neutrophilic cells and hyaline bodies, also a soft spleen, frequently with large cells resembling Türk's irritative forms, and iron-containing pig-

ment, the red bone marrow in the thigh with Charcot-Leyden crystals. Cirrhosis of the liver also causes increased excretion of uric acid in its early stage and the icterus is also an urobilin-icterus (cythæmolitic), frequently there exists anæmia. Thus we must admit a striking similarity of the disease with cirrhosis of the liver. Bleichroeder has never found convincing evidence of a primary disease of the hepatic cells in cirrhosis of the liver and is, therefore, inclined to include liver cirrhosis among the diseases of the blood. Perhaps there exists a uniform cause for the occurrence of the changes in the liver and the hæmatopoietic system.

HÆMORRHAGIC AFFECTIONS

BY
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TRANSLATED BY
DR. EDWARD F. WOOD, WILMINGTON, N. C.

UNDER the name of Hæmorrhagic Affections or Hæmorrhagic Diathesis a number of pathological conditions are grouped together which have in common a fundamental tendency to blood extravasations. These affections occur apparently more or less independently and are therefore to be differentiated from the secondary extravasations which occur as a sequel to other diseases. This line, however, cannot always be drawn sharply, there being rather a large number of transition cases which are difficult to group. Secondary hæmorrhages are for instance observed in infectious diseases, especially diphtheria, hereditary syphilis, septic processes, leukæmia, etc.

The tendency to hæmorrhages may be congenital and in that case habitual, a condition known by the name of hæmophilia, or it may only temporarily be present in particular individuals.

This latter group of transitory hæmorrhagic diatheses is represented by the various forms of purpuric affections: purpura simplex, purpura rheumatica, purpura hæmorrhagica, purpura abdominalis, purpura fulminans, further by scorbutus, infantile scurvy, melæna neonatorum and paroxysmal hæmoglobinuria.

Except for our increased knowledge of infantile scurvy (which has been treated in a different place) the last twenty-five years have not wrought any very startling changes in our knowledge of hæmorrhagic affections, since the epoch-making works of Immermann, Grandidier and Henoch. True, bacteriological investigations have here, too, exercised a stimulating effect, the more so as many of the observed purpura cases gave rise to the supposition that infectious processes were at the bottom of them. The search for a specific cause of purpura hæmorrhagica kept many investigators busy, but the results of the excellent work of Letzerich, Babes, Finkelstein, von Dungern, and others, are not yet satisfactory. Moreover the opinion represented chiefly by Giroux and Cattaneo has gained ground, namely that purpura is not an independent affection at all, but merely a symptom-complex caused by a number of different factors.

The old doctrine of Immermann regarding the diminished coagulability of the blood has experienced scientific examination and partial

confirmation by the recent investigations of Sahli. Therapeutically progress was made by the introduction of gelatin on the recommendation of Zuppinger and Baginsky; of adrenal preparations to control hæmorrhage; of atropine, to check impending intestinal symptoms (Hecker); and also by the precise study of hæmophile articular hæmorrhages by König which helped to put this affection, which has long been mistaken as "rheumatic," into its right place.

HÆMOPHILIA

Bleeders' disease, or the habitual tendency to hæmorrhages is in most cases congenital. It is considered the most hereditary of all diseases.

There are two types of "bleeders" according to whether the hæmorrhages occur after a trauma or apparently without cause: transitory bleeders or spontaneous bleeders. A sharp line of demarcation cannot be drawn, it being accepted as probable that even the second class owes its hæmorrhages to small traumata which had escaped attention.

Occurrence.—The first manifestations occur in most cases (about 65 per cent.) in infants under 2 years of age, very rarely in persons over 22 years of age. In infancy traumatic hæmorrhages are generally more frequent than spontaneous ones. The affection has a predilection for temperate latitudes, and Germany furnishes the largest number of cases. Boys have a much greater tendency to it than girls, according to Grandidier 13 times and to von Etlinger $3\frac{1}{2}$ times as great.

Heredity.—Although heredity in many patients cannot be demonstrated, in most of them the affection can be traced through several generations. In many families the ancestral taint has been present for over a century. For this reason there are usually a number of bleeders in one family, while sporadic cases are rare. While the male members of a family are affected much more frequently than the female ones, the latter have the peculiar ability of transmitting the affection to their offspring without ever having been bleeders themselves. Hæmophilic men generally procreate healthy children through women who have not sprung from bleeder families, whereas hæmophilic women as a rule produce children with the affection. Non-hæmophilic male members of bleeder families hardly ever procreate hæmophilic children. Exceptions however are known where the female members were particularly affected.

Some individuals or whole families display under certain circumstances a tendency to only spontaneous or only traumatic hæmorrhages.

Symptoms.—The long-continued existence and the difficulty of controlling these hæmorrhages is more characteristic than their severity, which is often not at all great. The hæmorrhage may last for days, weeks or months, the blood not spurting, but slowly oozing from the capillaries.

The traumatic hæmorrhages may occur into the interstitial tissue,

skin, muscles or articulations, where under certain circumstances they may assume the shape of large extravasations; or they may appear on the free surface of the skin or mucous membranes on the slightest provocation; irregularly torn wounds are more apt to give rise to obstinate hæmorrhages than smooth cut ones. Ritual circumcision seems to be especially fraught with danger in this regard; hæmorrhage of this kind has also been observed after paracentesis of the tympanic membrane (Thompson). Vaccination has given little cause for apprehension.

Spontaneous hæmorrhages are sometimes preceded by prodromata in the shape of vertigo, lassitude, sensation of cold or perspiration. The hæmorrhages occur either on the free surfaces of mucous membranes or into the subcutaneous cellular tissue. Among the former bleeding from the nose and the buccal cavity (on the eruption of the teeth) is frequent and specially dangerous. Bleeding from the umbilicus is surprisingly rare in bleeder families. The interstitial hæmorrhages of the skin, generally a very early and very regular symptom of hæmophilia, sometimes appear in the shape of petechiæ, sometimes of regular tumors (hæmatoma) in the subcutaneous cellular tissue (Neter). They are usually situated at the lower extremities and the lower part of the trunk. Their color differs according to age of the hæmorrhages from dark and bluish red to brown and light yellow. As a rule the petechiæ appear in crops, disappearing again completely by absorption. Fairly large blood extravasations may however cause suppuration which it is dangerous to incise as this may give rise to fresh bleeding and sepsis.

Complications.—Frequently in the course of hæmophilia there are hæmorrhages into the skin which indeed may be the only symptom; there are colorless, soft, elastic enlargements, generally at the knee and hip-joints, which were formerly regarded by patients and physicians alike as rheumatic affections. Even if these articular hæmorrhages usually terminate favorably by resorption, it may well happen that the simple hæmarthritic effusion changes to chronic panarthritis and its sequelæ—serious deformations and contractures (König).

Stiffness of the limbs may also arise from extensive interstitial hæmorrhages, which by connective tissue organization may lead to atrophy of muscles and tendons.

Etiology.—Practically nothing is known in regard to the causation of hæmophilia. This is sufficiently proven by the large number of hypotheses, none of which is supported by demonstrable facts. Lossen and Grandidier assumed a faulty mixture of the blood, causing impaired coagulability; Immermann assumed an augmented total quantity of blood, or pathological plethora; Virchow, congenital stenosis of the arteries and thinness of their walls; Aberhalden, an anatomical anomaly in the construction of the vessels differing according to localization; W. Koch, an infectious cause; Sahli, a disturbed chemism of the vascular

walls which being transmitted with the germ plasma would lead to abnormal friability and permeability. What has really been demonstrated in a few cases is fatty degeneration of the vascular intima, and enlarged endothelia with swelling of the nuclei (Virchow, Hooper, Linton).

The examination of the blood showed different degrees of diminished hæmoglobin, and microscopically the picture of severe anæmia with poikilocytosis and nucleated erythrocytes (Faludi). Sahli has latterly demonstrated that the polynuclear leucocytes are reduced both absolutely and relatively and that the quantity of fibrin and the physical properties of the blood are normal. The time of coagulation of the blood was normal at the time of the hæmorrhages, or possibly somewhat prolonged, while at the time when there were no hæmorrhages it was considerably protracted.

Gangrenous processes may be caused by the pressure of an extravasation in the interstitial tissue upon the neighboring parts. This causes atrophy either of small principal parts, or, when larger vessels are being compressed, of entire extremities.

Course and Prognosis.—A particular hæmorrhage may be checked either by artificial aid, or spontaneously by lowering the blood pressure. If the hæmorrhages continue for a long time, the blood becomes constantly lighter and thinner and death may supervene with manifestations of extreme anæmia. In other cases, however, the patient may rapidly recover in a relatively short time from even very severe blood losses, and just this tolerance of bleeders in the face of profuse blood losses is remarkable. A large proportion of hæmophilic patients, however, succumb early in childhood owing to internal and external hæmorrhages, 60 per cent. dying before the eighth year and only 11 per cent. reaching the eleventh year (Litten). The total mortality of hæmophiles is 87 per cent. (von Etlinger).

THE PURPURA AFFECTIONS

These are a series of disease pictures which have the one point in common that, in the shape of an independent disease, transitory and spontaneous hæmorrhages occur in internal and external parts; a transitory hæmorrhagic diathesis.

For a long time various forms of purpura have been distinguished; the recognition, however, has gradually gained ground that they all present the same pathological picture, differing merely in degree and localization: hæmorrhages of purpura simplex merely on the external skin; of purpura rheumatica, skin hæmorrhages with simultaneous involvement of the articulations; of purpura abdominalis, skin hæmorrhages with severe gastric and intestinal manifestations, perhaps also articular affections; of purpura fulminans, the gravest form of skin hæmorrhages; of purpura hæmorrhagica, or morbus maculosis Werlhoffii,

skin hæmorrhages combined with hæmorrhages of the mucous membranes or into internal organs. All these forms cannot be strictly separated, clinically, etiologically or anatomically. One form may coexist with another or change into it. From this point of view the divisions used in the following pages should be understood.

Occurrence.—Purpura is rather a rare disease, principally affecting children after the third year; infants are almost entirely spared. Förster observed an average of 1 case in every 1300 out-patients. Girls seem to be somewhat more predisposed to it than boys; there are more cases in winter than in summer. According to C. Koch's statements concerning the frequency of purpura in St. Petersburg, the influence of some local tendency may be supposed to be at work.

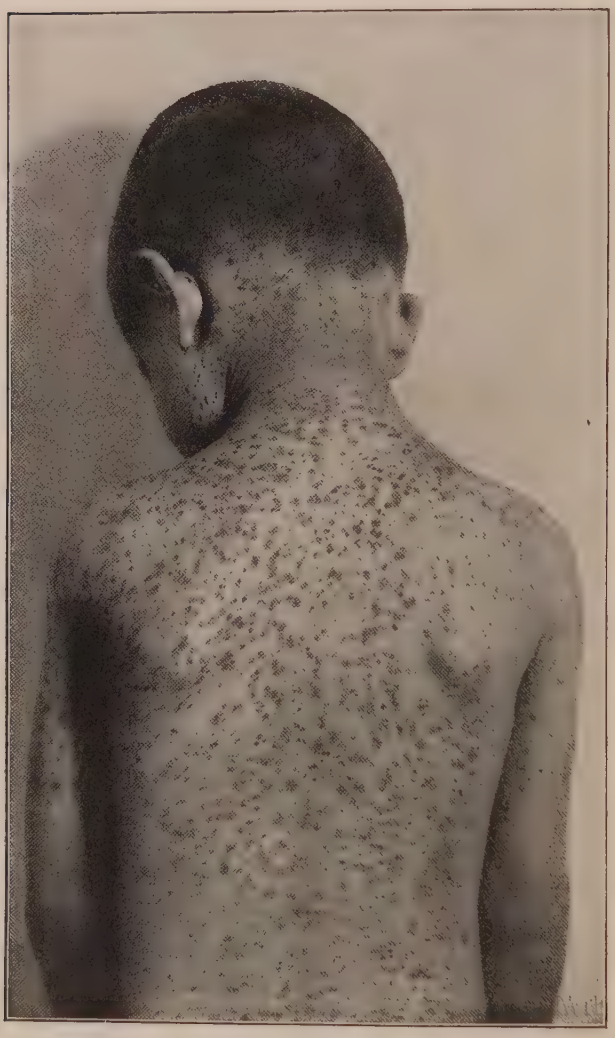
Etiology.—Although certain factors must certainly be considered as indirect causes, such as weak constitution, chronic anæmia, chronic intestinal catarrh, unhealthy dwellings, malnutrition especially by starch and preserved food, a direct cause cannot be stated at the present time. With great probability and in some cases with certainty it may be assumed that infectious processes are present. The attempts, however, to point to a specific causative factor have so far been doomed to failure and will probably so continue, it having been found that bacteria of different types may under certain circumstances produce hæmorrhagic affections. Successful experiments have been made to obtain pure cultures of various bacteria from both the maculæ and the blood of purpura patients and to reproduce hæmorrhagic diseases therewith in animals, for instance streptococci (Hochheimer), staphylococci ("staph. cereus albus" Fiorentini), colon-like rods (Benedetti), bacillus pyocyaneus (Neumann, Hecker), bacillus purpuræ (Letzerich, Gimard, Kolb, Babes), capsule diplococci (von Dungern), and a bacillus resembling that of mouse septicæmia (Finkelstein). Anything specific however can probably not be attributed to any of these bacteria. Typical purpura has been observed in the course of, and following leukæmia, diphtheria, and especially of angina lacunaris (Bruck). The opinion held by Giroux and Cattaneo that purpura is not an independent disease but a symptom-complex, continues to gain ground, and it is quite possible that such symptom-complex may also be produced by non-bacterial causes such as chills, alcoholism, overexertion, although even in these cases a latent infection cannot be excluded.

The manner of the occurrence of these hæmorrhages is equally obscure. In cases where bacterial embolisms are present—and these form the majority—we must not content ourselves with the assumption of a toxic influence upon the capillary walls which favors a diapedesis of the red blood. Diminished coagulability of the fibrin which had formerly been supposed to exist, cannot be demonstrated either chemically or microscopically.

Anatomy.—Accordingly, the anatomical yield is small. In grave cases of purpura hæmorrhagica there are parenchymatous degenerations of heart and liver, also hypoplasia of the bone marrow (Muir).

In milder cases the blood shows a diminution of the white and red blood corpuscles, of the hæmoglobin and of the specific gravity; in grave cases (purpura hæmorrhagica) considerable leucocytosis, poikilocytosis and microblasts.

Fig. 29.



Purpura simplex.

PURPURA SIMPLEX

Purpura simplex is characterized by slight blood extravasations into the skin only. These appear quite unexpectedly, or they are anticipated by certain precursors several days in advance, such as headache, anorexia, lassitude, vomiting. The maculæ have the size of a pinhead to a lentil, are of circular shape, resembling fleabites or weals; they are isolated and do not coalesce. The fresh maculæ are dark red or bluish red, after some time they become paler and pass through the various stages of the blood-pigment. In some of them there is a palpable indurated spot in the centre (fibrinous coagulation). They do not disappear on pressure. In their distribution they show a predilection for certain parts of the body; thus the face and usually the hands also are left free, while a preference is shown for the extensor surfaces of the lower extremities and the arms; as they extend further, they invade also the trunk. The eruption occurs either all at once or advances by jumps.

In the latter case macules of every age may be noticed side by side.

The *general condition* is usually not disturbed at all; prodromal manifestations, should such exist, usually disappear with the eruption. Fever, as a rule, is absent.

There are sometimes deviations in the exanthem to such an extent that the petechiæ are infiltrated like œdematous wheals—purpura urticans (Biedert). Further, a true urticaria or exudative eczema may develop side by side with the maculæ of the purpura.

Course and Termination.—The duration of the pathological process depends upon whether the petechiæ appear practically at the same time or at more or less distant intervals. In the former case eight to twelve days are reckoned to effect a cure, in the latter case it may require weeks or months. The termination is always favorable; only where there is considerable extension of hæmorrhage and a prolonged duration of the affection, there may be manifestations of anæmia.

PURPURA RHEUMATICA. PELIOSIS RHEUMATICA
(Schönlein)

When purpura simplex is complicated by articular pains and swellings which dominate the disease picture, it is termed purpura rheumatica.

Symptoms.—The affection frequently commences with certain prodromal signs: lassitude, anorexia, also vomiting or diarrhœa, vague pains in the limbs which are not yet localized at the joints, sometimes urticarial eruptions. Then fever sets in, followed by the appearance of the red macules. The latter are usually a little larger than in purpura simplex, do not coalesce, and are generally found only on the legs up to just above the knee, but may also appear in other places. They are always most numerous in the neighborhood of the joints of the extremities. Sometimes they protrude above the level of the skin, the extravasation on account of its hardness being palpable.

The articular pains and swellings appear either before or after the eruption, the joints of the feet and knees being affected most frequently. The œdema is caused by serous infiltration of the periarticular parts. Thus there is no question of articular inflammation as in articular rheumatism, or of hæmorrhages into the joints as in hæmophilic articular affections. Both the absence of any cardiac involvement and the regularly favorable termination of these articular affections form further differentiating points as against the other two affections named.

Frequently not only the joints, but also the bones of the lower extremities are painful on pressure.

A peculiar point, also shared with purpura simplex, is the not infrequent combination of the petechiæ with other skin affections, such as erythema nodosum, multiform exudative erythema, urticaria, etc.,

so that the nodules of erythema nodosum may, for example, change to blood extravasations or the urticaria wheals may be filled with blood (Neter).

In the course of the disease there are frequent collections of œdema, especially at the lower extremities, the scrotum, elbows and eyelids, although no albumin is demonstrable in the urine.

The *general condition* is but slightly disturbed on the whole, but elevations of temperature up to 40° C. (104° F.) have been observed.

FIG. 30.

Purpura rheumatica. Girl aged one year and nine months. Acute onset with articular swelling and skin hæmorrhages at the trunk and extremities. Spots up to lentil size and especially numerous at the œdematous joints. The œdema around the ankle-joints is continued to the root of the toes.

Course and Termination.—In acute cases with rapid onset the affection lasts about fourteen days, usually however it takes a paroxysmal course, so that a few days after the disappearance of the manifestations there appear fresh eruptions with renewed fever and other articular swellings. These relapses are especially encouraged by patients leaving the bed too soon. The termination is always favorable.

PURPURA HÆMORRHAGICA. MORBUS MACULOSUS WERLHOFII

The hæmorrhages occur not only on the external skin and in the subcutaneous cellular tissue, but also in various mucous membranes and in the internal organs.

The affection usually begins quite suddenly without prodromata while patients are in the best of health, by the appearance of blood spots over the entire trunk and the extremities. These spots are partly similar to those in purpura simplex, but most of them are considerably larger up to the size of a small dish and coalesce into large patches. Their contour is irregular, partly round, partly oval and partly striated; color dark red with bluish or brownish tint; and the body attains quite a peculiar tiger-like appearance. Here and there the hæmorrhages assume the form of subcutaneous infiltrations. In severe cases, where the blood spots coalesce to a considerable extent, the particular extremity appears quite dark, œdematous, and covered with wheals similar to gangrene, except that the odor is absent. Sometimes the hæmorrhages extend over small areas, but invade deeper layers and form coarse knots.

Fig. 31.

Purpura hæmorrhagica. Eight-year-old girl; acute attack with fever. Dark, bluish red blood spots as large as half a dollar to a small plate in the skin of the upper and lower extremities. The malar mucous membrane likewise shows small punctiform hæmorrhages. Cure after 3½ weeks.

These skin hæmorrhages are associated with hæmorrhages from all kinds of mucous membranes, especially from the nose. Epistaxis is one of the regular symptoms of the affection. Then there appear blood spots on the mucous membranes

of the lips, palate and tongue, less frequently on the conjunctiva or in the ear. Hæmorrhages on the mucous membranes of the intestine and the bladder are shown by the excretion of bloody stools and bloody urine, but, like hæmoptosis and hæmatemesis, this occurs only in very rare and very severe cases. The joints, as a rule, remain uninvolved.

There is such a pronounced general tendency to hæmorrhage that slight pressure on any part of the body suffices to produce an extravasation of blood into the skin, the subcutaneous cellular tissue, or the joints. In slight external injuries occasioned by scratching with the fingernails, injections, punctures in blood examinations, there are often hæmorrhages which may become dangerous on account of the difficulty to control them.

The *general condition* is sometimes disturbed only slightly but in many cases very perceptibly: the children are ill-humored, fagged out, tired, ask to go to bed, complain of headache and look pale. In severe cases an almost typhoid condition may be developed. The temperature is not materially elevated as a rule, but under certain circumstances may rise to 39.5° C. (103° F.) in the evening. Pulse sometimes slow. More serious disturbances of the general condition will then appear, if severe and frequent epistaxis has caused profuse loss of blood. The debility may then become pronounced.

Course and Termination.—The majority of cases have an acute course without any actual repetition of the attacks. When the spots have reached the climax in point of number and extent, which is generally the case in about a week, they become paler and change color along with the changes of the blood-pigment. The frequent bleedings from nose and mouth come to a standstill, feces or urine which may have been tinged with blood, resume normal conditions and after about fourteen days recovery is complete.

Sometimes, however, the onset is slow, and then the affection takes a much more chronic course. The hæmorrhages on the skin, from the nose and gums, etc., are so frequently repeated that many weeks and months may elapse before a cure is effected. In fact, when the intervals of apparent health are of longer duration, the trouble extends over several years. These are the cases which owing to considerable loss of blood may lead to grave conditions and even death. On the other hand, cases have been reported which in spite of an acute course have ended fatally within a few days. On the whole, however, the termination is favorable.

ABDOMINAL PURPURA (Henoch)

In the course of a rheumatic purpura abdominal manifestations, such as vomiting, intestinal hæmorrhages and colic may appear under certain circumstances. These are productive of a peculiar symptom-

complex which Henoch observed in several cases in 1868 and described in 1874. Since then a number of these cases have been published. The course is generally as follows: Sometimes after macules and œdema have existed in various joints, certain dyspeptic complaints occur, the articular pains become more severe, and new blood extravasations make their appearance. Vomiting is exceedingly obstinate and difficult to control, the vomited matter consisting of colorless or greenish mucus at first, and changing later to dark bloody masses. Attacks of violent colicky pains torment the patient to such an extent that he groans and cries out in his bed. The pains generally increase until a defecation has taken place, which is generally accompanied with considerable tenesmus. The stools at first scant and hard, become diarrhœal, assuming a blackish, dark red or orange yellow color. Anorexia is complete. In consequence of the pains, vomiting and loss of blood, patients become rapidly debilitated and give the impression of being seriously ill.

The objective signs may be multiform small and medium-sized petechiæ, œdema, painfulness and stiffness of the knee and ankle-joints, sometimes also of the elbow-joints. The articular regions are likewise the seat of the densest macular eruptions. The abdomen is distended and usually highly sensitive to pressure in the region of the transverse colon. There is fever, which however does not exceed 38.5° C. (101° F.) as a rule. The buccal cavity remains free from hæmorrhages; there are no cardiac changes.

Like all forms of purpura, the abdominal variety is particularly characterized by paroxysmal manifestations with intervals of days, weeks or even a year, which tend to protract the illness considerably. The attacks themselves gradually diminish in vehemence, or the relapses may concern only the blood spots or only the articular swelling. Aside from these fully developed cases there are others in which one or other of the symptoms is absent, for instance the articular swelling.

Henoch's purpura, like all other forms of purpura, should not be treated as an affection sui generis, there being only a question of specific localization of the affection in the area of the intestinal tract. No anatomical observations in children have been reported, but the assumption of blood extravasation into the mucous membranes of the stomach and intestine will probably not be far wrong. It is an undecided point as to what makes the intestine so sensitive. In the case of a ten-year-old boy observed by the author the habitual consumption of alcohol (son of a restaurant keeper) and marked errors of diet were held responsible for the cause of the first attack and the following relapses.

The **prognosis** is always to be made with caution on account of the grave condition and the impending danger of nephritis.

PURPURA FULMINANS

This affection, which was likewise first described by Henoch, represents an exceedingly rare, but the gravest, modification of purpura simplex. While hæmorrhages from mucous membranes are absent, extensive ecchymoses develop with alarming rapidity. They appear bilaterally and rather symmetrically, discoloring entire extremities within a few hours, first bluish red, then blue and black-red, and causing a coarse blood infiltration of the cutis. There is often a formation of serosanguineous vesicles upon the skin, but never gangrene, nor is there any fetid odor. The course is alarmingly rapid and always fatal; within 12–24 hours from the formation of the first blood spot death supervenes; the longest period was four days. There are no complications, autopsy yielding a negative result with the exception of general anæmia. In a few cases there are reports of a history of preceding acute infectious diseases, in others however there was a total absence of etiological indications.

SCORBUTUS

Scurvy is a transitory hæmorrhagic diathesis which is associated with severe disturbance of nutrition, and with a tendency to ulceration and ichorization. In childhood it certainly occurs rather rarely. Möller-Barlow's disease which by many is termed infantile scurvy, and true scorbutus should be considered distinct.

Etiologically there may possibly be certain infectious causes such as streptococci and staphylococci, but the essential condition is a body prepared for the development of scurvy by improper nutrition and unhygienic conditions. Food poor in vegetable acid alkalies is held especially responsible (Immermann): long-continued nutrition with flour-foods, condensed, preserved or sterilized milk, inferior bread, want of fresh vegetables, fruit, fresh meat. A further necessity for the development of the affection seems to be continued living in dark, ill-lighted, damp dwellings.

Symptoms.—The affection never begins suddenly, but always slowly, exhibiting signs of gradually advancing cachexia, emaciation, pallor of the skin and mucous membranes, disturbances in the cardiac and intestinal functions. To this is added a specific scorbutic affection of the gums; extensive painful swelling, and loosening of the gums, which bleed at every touch, also loosening of the teeth. Frequently there is necrotic disintegration of the marginal parts, which become desquamated and form a slate-colored, ulcerating gray surface.

To complete the pathological picture, there are numerous petechiæ and ecchymoses into the skin, the connective tissue and muscles, on mucous and serous membranes, in the periosteum and on the retina. There is also actual bleeding, especially from the nose; feces and urine tinged with blood are less frequent. Enlargement of the spleen may also develop.

Blood Findings.—Examination of the blood does not disclose anything really characteristic. Corresponding to the losses of blood there is a diminution of hæmoglobin and red blood corpuscles. Hayem, Robin and Pentzold observed small corpuscles resembling blood platelets of strong refractive power.

Course and Termination.—Scorbutus always takes a chronic protracted course, but there is no accentuation of paroxysmal attacks. Mild cases may be cured, severe ones frequently terminate fatally, as a rule in consequence of complications, ulcerations, septic processes, pleuritis, pericarditis. The prognosis is therefore doubtful.

PAROXYSMAL HÆMOGLOBINURIA

Hæmoglobinuria from cold; Psychogenic Hæmoglobinuria.

In this affection there are paroxysmal secretions of dark blood-colored urine, with or without ascertained causes. It should be distinguished from hæmoglobinuria of the newborn (Winckel's disease) and from symptomatic hæmoglobinuria which occurs after burns, poisoning with phosphorus, chlorate of potash, mushrooms, and has no paroxysmal character.

Symptoms.—The attack is usually preceded by a state of general irritability, lassitude, yawning; the attack itself sets in with chills, sensation of great cold, cyanosis, promptly followed by a state of heat and perspiration. Sometimes there is even collapse. Then there is a secretion of blood-colored urine, at first usually accompanied by severe pains. Frequently there are hyperæmic spots appearing simultaneously on the skin, especially in parts affected by the cold, sometimes there are wheals. A few patients exhibit under certain circumstances gangrene at various parts of the body.

The urine is either blackish, dark red, burgundy or claret colored, but always dark colored. It contains abundant albumin, gives Heller's and Almen's blood test, but in the microscopic picture blood corpuscles are absent. On the other hand, there are brownish, lumpy masses. In the spectrum it shows the bands of methæmoglobin.

The blood in the first paroxysm shows hæmoglobinæmia, the serum containing hæmoglobin; there are also pale erythrocytes and so-called shadows (Burkhard). After the paroxysm both hæmoglobin and red blood corpuscles are diminished. The blood, however, recuperates very rapidly, so that on the following day the examination shows the blood already normal. During the interval between paroxysms there are never traces of hæmoglobin in the blood serum.

Etiology.—As a predisposing factor there is at the bottom of many cases a previous chronic or acute infectious disease, especially hereditary syphilis, malaria, scarlet fever, and as immediate cause there is almost always a severe chill or thorough wetting; hence the appellation

cold hæmoglobinuria. Infectious factors do not appear to have any influence, this being probably a neurosis which chiefly affects the vasomotor system (von Recklinghausen).

Probably the chill causes primarily a change in the chemico-biological composition of the plasma enabling it to exert a hæmolytic influence upon the blood corpuscles. Especially suitable to the production of hæmolysis is cold in conjunction with congestion. It is possible to produce by artificial experimentation hæmoglobinæmia and in specially predisposed persons also hæmoglobinuria, by cutting off the blood supply of a finger and after a while dipping the finger into cold water (Ehrlich's experiment), or by giving the patient a cold foot bath.

Course and Prognosis.—A single paroxysm generally lasts 1½ to 2 hours. The paroxysms are repeated in irregular intervals according to the possibility of exposure to cold, and they are more frequent in winter than in summer. The prognosis depends upon the nature of the original trouble, but is on the whole favorable.

DIAGNOSIS FOR HÆMORRHAGIC AFFECTIONS

The recognition of fairly pronounced cases is easy. The strict diagnostic separation of the various forms of purpura is without practical importance; in case of need a review of the points mentioned on page 172 in regard to the uniformity of the various forms of purpura ought to be sufficient. An early recognition of hæmophilia would be important, as the life of the patient may thereby be prolonged for years; but unless there is a bleeder family in the case, the diagnosis is difficult and probably only possible after the first serious hæmorrhage. Frequent recurrence of "rheumatic" pains in limbs and joints requires careful observation if it occurs in a member of a bleeder family, as the pains may exist for a long time as the only expression of a latent hæmophilic diathesis. Considering that these articular affections represent so to speak a *noli me tangere*, it is necessary to differentiate them from other similar affections. They are most easily confused with tuberculous white swelling, from which they may be distinguished by the rapid appearance and disappearance of the exudates and by the absence of any considerable thickening of the capsule.

Hæmophilic articular affections as well as articular swellings in rheumatic purpura are distinguished from *articular rheumatism* by the larger swelling in the latter, the local development of heat, the moist skin tending to perspiration and fever. It should be understood that in hæmophilia there are hæmorrhages into the joints, that in purpura there is œdematous swelling of the periarticular parts, that in rheumatism there is inflammatory swelling and effusion into the joints and their neighborhood, that in tuberculous arthritis there is granulation which always considerably involves the adjacent bones. In all these

cases X-ray examination will prove a most excellent aid in diagnosis.

Morbus Maculosus and Scorbutus.—These two affections are different in their very onset. In the former it is more or less sudden, in the latter after slow preparation of the soil. Although in the course of purpura hæmorrhagica a severe disturbance of nutrition may set in, it is always a secondary occurrence and never present simultaneously with the first appearance of the other manifestations; such however is the case in scorbutus, in which along with early disturbed nutrition, there is a characteristic tendency to ulceration and inflammation. The affected gums in scorbutus are known by their dark red swelling, their spongy consistency, the loosening and sensitiveness of the gums, all manifestations which are absent in purpura.

The urine in *hæmaturia* is distinct from that in *hæmoglobinuria* by its *lake-colored* appearance and the percentage of the red blood corpuscles; in the latter disease attention should be paid to the paroxysmal occurrence in conjunction with the effect of cold. Hæmaturia occurs, aside from hæmorrhagic diatheses, when there are stones in the bladder, the renal pelvis or the kidney, a condition generally associated with considerable secretion of mucous and inflammatory products in the urine.

TREATMENT OF HÆMORRHAGIC AFFECTIONS

Hæmophilia.—Correct prophylaxis should endeavor to restrict the procreation of hæmophilic children. According to Grandidier's experience it is well to discountenance marriage of female members of bleeder families, whether they themselves are bleeders or not; male members, however, unless they are bleeders themselves, may be permitted to marry. Male bleeders should only then be dissuaded from marrying if there is proof that in their families hæmophilic men have procreated hæmophilic children, always provided that the males in question had married healthy daughters of healthy families.

Individual prophylaxis should commence immediately after birth, and in view of the dangerous character of the hæmorrhages be carried through with persistency during the first few years of life. Every injury, be it ever so slight, should be prevented; for this reason all surgical interference is contraindicated, as for instance operation for cleft palate, removal of nævi, piercing of earlobes, and particularly circumcision. Vaccination, however, has always proved free from danger. Taking great care of the buccal cavity, preventing as far as possible the extraction of teeth, and selecting toys, furniture and articles for domestic use with circumspection, are important. In later life caution at beginning of menstruation, interdiction of gymnastic exercises, selection of a suitable vocation, are points commanding attention.

The general treatment should endeavor to strengthen the entire organism, for which purpose a mild diet with plenty of fresh vegetables

and salad should be prescribed, avoiding articles which excite the vascular system, such as alcohol, coffee, tea. Cold friction, saline baths, residence in the country or at the seaside, are efficacious adjuvants.

Internally, vegetable acids (lemon cure) may certainly be tried, although the success is doubtful. The same applies to the administration of saline remedies or the reduction in the supply of fluids recommended by Immermann and Oertel on account of plethora which they are supposed to excite.

The special treatment of the hæmorrhages consists in the first place in elevating the affected part of the body, which is often sufficient. In the second place apply compression, tamponade, the cautery, compression or ligation of the nearest vascular trunks. For a local hæmostatic the custom now is to apply, aside from chloride of iron, the adrenal preparations: adrenalin or suprarenin in solutions of 1 : 1000. Hesse recommends a solution of calcium chloride. Good results have been obtained by gelatin treatment, injecting 25 Gm. (℥vi) of Merck's 10 per cent. "Gelatina Sterilisata pro Injectione."

The treatment of hæmophilic articular affections consists in rest and moderate compression; when the pains are severe apply moist packing, from the second or third day massage of the centrally situated parts. As to operative interference nothing but aseptic puncture is admissible. Later on orthopedic measures may become necessary.

Purpura.—In view of the uncertain etiology of purpura there can be no question of causal treatment. The foremost measure is thorough.

General Treatment.—In all cases, even the mildest, strict rest in bed is necessary. But this very requirement frequently meets with great objection, because the patients, enjoying otherwise good health, can be kept in bed only with difficulty, while parents are not easily convinced of the necessity of the measure. It should be remembered that the frequency of relapses is usually due to failure to observe these instructions. The sick room should be well ventilated and kept cool. The diet should be bland, not seasoned; all exciting substances,—alcohol, coffee, tea,—should be avoided and the preference given to milk, light farinaceous dishes and vegetables. Large meals are injurious; instead, small portions should be given every two or three hours. Constipation, which may readily occur, should be overcome by the use of grated apples, senna-infusion, castor oil. Highly indicated are regular baths, to which decoctions of oak bark and walnut leaves have been added, as they contribute to the more rapid resorption of skin hæmorrhages. In very protracted cases a change of climate is often useful. As an after-cure, a general strengthening of the body is necessary and a stay in the mountains or at the sea-side advisable. Special attention is frequently demanded by secondary anæmia, the treatment of which is to be conducted according to the usual rules.

The special treatment is purely symptomatic. The hæmorrhages cease of their own accord with quiet rest in bed. In epistaxis prescribe horizontal position with lowered head, compression of the affected ala, sniffing up cold water in which a few drops of chloride of iron solution has been mixed, and tamponade. In internal hæmorrhages, no time should be wasted over ergotin, which is uncertain in action; there should be immediate and repeated injections of 20–30 c.c. (℥v–℥i) of a 10 per cent. gelatin solution; for internal administration up to 200 Gm. (℥vi) daily of the same solution may be given. Treatment of the abdominal symptoms, such as occur in mild degrees in morbus maculosus, and in the gravest degree in Henoch's purpura, demands special attention. Here absolute rest, application of the icebag on the abdomen and strictest diet are in order. Cooled milk, cold albumin water, cold almond milk, should be given by the teaspoonful, until the stormy manifestations have come to an end. Intestinal hæmorrhages should be checked by a diluted solution of iron chloride given by the teaspoonful, gelatin subcutaneously or internally. For the pain give opium. The success of these remedies, however, is by no means positive. In a grave case in my practice atropine rendered excellent service. The pains as well as the hæmorrhages ceased instantly after an injection of 0.0003 Gm. ($\frac{1}{200}$ gr.) atropine sulphate. The remedy has not only an instantly antispasmodic action, but evidently an ischæmic effect upon the intestinal vessels. Rectal irrigations with a 1 per cent. solution of lead or aluminum acetate are recommended.

Scorbutus.—By way of prophylaxis infants should be fed as long as possible on mother's milk; otherwise fresh, raw or recently boiled milk should be given, also fruit juice. Older children receive raw milk, plenty of fresh vegetables, fruit and salad. Generally speaking, an improvement of the hygienic conditions should be attempted. These measures are also applicable to the removal of already existing symptoms.

Internally cinchona preparations, myrrh, yeast preparations (zymin, lævurinose and others) may be tried.

The scorbutic affection of the gums is treated locally with astringents, painting with weak solutions of silver, aluminium acetate, alum, chlorate of potash, potassium permanganate or tincture of myrrh; older children rinse their mouths with a decoction of oak bark or cinchona. The skin ulcers require antiseptic bandages (potassium permanganate), avoiding surgical interference.

Hæmoglobinuria.—During paroxysms, rest in bed, warmth, avoidance of lowering body temperature, bland diet, plenty of milk and water, warm baths. In the intervals, strengthening of the body, protection against colds and overexertion. Should there be a recognized cause, hereditary syphilis or malaria, then the medication should be directed against this by antisyphilitic or quinine treatment, respectively.

INFANTILE SCURVY

BY
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TRANSLATED BY
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(Synonyms.—Barlow's Disease, Möller-Barlowsche Krankheit. Skorbut der kleinen kinder. Infantile Scurvy. Scorbut infantile.)

Definition.—By the term infantile scurvy is understood a scorbutic affection occurring in the early years of life, and characterized chiefly by marked anæmia of the skin and mucous membranes, bleeding gums, pain upon movement and the occurrence of swellings upon the long bones of the extremities and upon the ribs. The anatomical basis of this disease is a specific affection of the bone marrow associated with anæmia and the hæmorrhagic diathesis. In the majority of cases the disease appears in association with a pre-existing rachitis of slight or severe grade, but it may occur entirely independently.

History.—Möller (1859 and 1862) first described it under the name "acute rickets," as he believed the specific symptom-complex was an indication of an acute exacerbation of rachitis, though Förster was inclined to assign to it an independent position. Ingerslev (1871) and Jalland called it scurvy, though some English authorities, especially Cheadle, laid great stress upon its association with rachitis. Barlow (1883) first brought to bear upon the subject numerous pathological as well as clinical observations; he regarded the affection as scorbutic and strongly emphasized the importance of dietetic therapy. When once the attention of physicians was turned to the question, reports appeared from many countries: from North America, Holland, Denmark, North Germany, later South Germany, France, Belgium, Sweden, Austria, Switzerland, Italy, Finland, etc. The American and French physicians called the disease scurvy, those from other countries generally Barlow's or Möller-Barlow's disease. Heubner wished to avoid the designation scurvy, as he regarded the conception of scurvy as poorly defined and because it does not usually occur where infantile scurvy is frequently observed, and furthermore, the symptom-complex of infantile scurvy differs decidedly from that of the adult type of scurvy. In addition to Barlow, we are particularly indebted to Naegeli, Jacobsthal, Schoedel-Nauwerk, Schmorl and Fränkel for the demonstration of the finer histological changes in this disease.

PLATE 9.

I. Lower leg, 9-months infant. *a*. Subperiosteal hæmorrhage over tibia ; *b*. smaller hæmorrhage over lower end of fibula.

II. Femur, same child. *a*. subperiosteal hæmorrhage ; *b*, juncture of shaft and epiphysis ; *c*, hæmorrhage in marrow.

III. Femur, fracture of upper end of the diaphysis, separation from epiphysis. *a*, periosteal new bone tissue.

IV. Section of broken rib in process of healing. *a*, subperiosteal hæmorrhage ; *b*, periosteal callus.

Occurrence.—Infantile scurvy is distinctly an affection of artificially fed children and though it has greatly increased in frequency in the last twenty to thirty years, it is yet rather rare.

Of one hundred cases, the ages at the beginning of treatment were as follows:

1	case	4	months
1	"	5	"
10	"	6	"
10	"	7	"
20	"	8	"
17	"	9	"
13	"	10	"
11	"	11	"
7	"	12	"
7	"	13–18	"
3	"	19–24	"

Isolated cases have been noted throughout the third and fourth years; the oldest case, six and one half years, was autopsied by Fränkel. Boys seem to be affected somewhat more frequently than girls. The influence of season is uncertain. The occurrence of cases in England, Holland and Northern Germany speaks for a geographical and climatological influence though cases occur in all countries. Favorable social conditions predispose to the occurrence of cases.

Clinical Picture.—The symptoms develop gradually and at first are not characteristic. The following is a typical clinical history:

A child in good surroundings; sunny dwelling, garden, careful attention; nourishment, artificial with Gärtner's "Fat milk." Child thrived until the ninth month, then had frequent slight digestive disturbances; then was less active than formerly, and dull. There was an increasing pallor of skin and mucous membranes, movements of the body were avoided; the child cried very frequently when handled. Legs were held as if paralysed. About the upper incisors the gums were much swollen and were of a bluish red color and bled easily.

The attending physician made a diagnosis of rachitis and ordered codliver oil and phosphorus, and salt baths. The child's condition grew worse under this treatment and it was therefore brought to the hospital.

Condition on admission, November 11, '03: a very anæmic but moderately well nourished girl of eleven months lies immovable on the bed and cries as one approaches it. No signs of rachitis. In the region of the upper and lower middle incisors marked hæmorrhagic swelling of the gums; at the lower end of the left humerus there is a diffuse painful swelling and similar ones are present over the lower third of the right femur and the lower half of the tibia. No special changes in heart or lungs. Temperature 38.5° C. (101.3° F.).

Blood examination shows: hæmoglobin 50 per cent. (Gowers); slight poikilocytosis, marked lymphocytosis, no abnormal forms.

Diagnosis.—Infantile scurvy.

Dietetic treatment with raw cow's milk, meat juice and fruit juice.

Course.—After four days there was a decided improvement of all symptoms, the child's whole condition changed; after fourteen days more it was almost well and was taken home. Uneventful recovery.

Symptoms.—The majority of the symptoms were present in the above case.

1. *Anæmia.*—Children formerly bright and rosy become gradually anæmic and finally waxy-white. The examination of the blood shows a fall in the hæmoglobin content to as low as 40 per cent., a marked decline in the number of erythrocytes, slight poikilocytosis, and leucocytosis with a decided increase in the mononuclear at the expense of the polymorphonuclear forms (Ritter); thus relatively insignificant blood changes with absence of abnormal forms. The view advanced by Senator that the anæmia is the result of a primary disease of the bone marrow is not justified by the pathological changes found in the marrow and the blood.

2. *Pain on Movement.*—At first the children cry very often with the ordinary handling, then move less than formerly and finally every movement or even a touch is painful. Movements of the legs are at first the most painful, and upon careful investigation one finds especial tenderness at the ends of the diaphyses; finally the legs lie immovable, as in syphilitic pseudoparalysis. The thorax also is very frequently tender, the arms less often so. This tenderness of the bones may be absent notwithstanding other well-marked symptoms of infantile scurvy. The tenderness which often extends over the whole body is dependent upon pathological changes in the bones and less upon a general hyperæsthesia.

3. *Enlargement of the Bones.*—Swollen areas appear upon one or more bones, most frequently at the lower end of the femur, so that these bones seem locally enlarged, and over them the skin becomes tense and glistening and the swollen part feels doughy to the touch. The swelling seldom reaches above the lower third or at most the middle of the femur. Frequently both thighs are involved. No less frequently the osseo-cartilaginous junction of the ribs is enlarged so that the picture of a rachitic rosary appears, and confusion with rickets may arise. In severe cases of rib involvement a separation of the cartilaginous from the bony portions of these bones occurs, so that the sternum and adjacent costal cartilages sink bodily backward. This phenomenon is almost specific for the disease.

Barlow says concerning this: "The sternum with adjacent costal cartilages and a small portion of the contiguous ribs appear as though they had been fractured by a blow from the front and had been forced backward."

The legs swell similarly to the thighs, and in association with the enlargement at the upper end of the tibia there is often found a swelling of the entire lower leg. These painful swellings may appear on the humerus as well as on the bones of the forearm, the scapula, the jaws or any bone of the body. After they remain for a time the skin over them assumes a bluish or bluish red discoloration. Not infrequently with or without these enlargements, evidences of interruption of continuity, crepitation and displacement, appear at the ends of the diaphyses of the affected bones.

4. *Hæmorrhagic swelling and softening of the gums* is a very important and frequent symptom. The dark bluish or purplish spongy gum closely surrounds and overlaps the teeth and shows a tendency to bleed. There is however, no tendency to destruction of the gums as in ordinary scurvy. This hæmorrhagic change is noted only about the teeth which have already appeared or around those which are about to come through; in fact, in the depths of the tumefaction one often sees the points of teeth which first show themselves as the swelling subsides. In children without teeth this change is either not seen at all or only just before the teeth are cut.

5. *Hæmorrhagic swelling of the Eyelids and Exophthalmus.*—Subperiosteal extravasations of blood appear also upon the cranial bones especially upon those of the orbit; they may press the eyeballs forward, and through infiltration of the blood into the loose tissues of the lids may cause the latter to become much swollen and of a bluish red color. This frequently affects both eyes and produces a marked disfigurement of the child.

6. *Extravasations of blood* into the skin and mucous membranes are seen as further evidences of the hæmorrhagic diathesis, but on the whole, they are less frequent and are but slightly characteristic. Thus there are small and larger hæmorrhages under the skin, usually in locations subject to irritation or in scars, hæmorrhages into the oral mucosa in addition to the gingivitis, into the conjunctiva, the nasal mucosa, and that of the intestinal tract (bloody stools).

7. *Hæmaturia* occurs in ten per cent. of the cases (Heubner), and is sometimes the only evidence of the hæmorrhagic diathesis. The urine shows a large amount of albumin, numerous erythrocytes and granular and red corpuscle casts; a true hæmorrhagic nephritis is rare.

8. *Fever.*—The temperature in about fifty per cent. of the cases is slightly elevated without definite type, and in general seldom rises above 39° C. (102.2° F.). The duration of the fever is very variable; feverish periods alternate sometimes with those of normal temperature.

No characteristic symptoms referable to the other organs occur. The respiration is frequent on account of the marked anæmia, the pulse is accelerated, the heart is sometimes dilated and anæmic murmurs may

be heard. The appetite is poor; the bowels are normal, or sluggish, though there may be diarrhœa with traces of blood-tinged mucus, especially if the hæmorrhage into the intestinal mucosa stimulates peristalsis. Bronchitis, pneumonia and severe intestinal catarrh are frequently met with as complications.

The **course** is decidedly chronic. Weeks or months are required for the full development of the clinical picture, and then the condition fluctuates backward and forward until death supervenes, apparently from cardiac weakness often aided by a complicating enteritis or pneumonia. Or a correct diagnosis leads to proper treatment and saves the life of the child. Without this the children usually die; the very slight cases may recover spontaneously. Apparently in many early cases, perhaps just beginning, a simple change in diet undertaken because the children were pale and dull, leads to recovery without infantile scurvy being suspected.

Pathology.—Naegeli, Schoedel-Nauwerk, Schmorl and Fränkel agree that the pathological changes in infantile scurvy consist chiefly in a characteristic affection of the bone marrow which is most marked at the osseo-cartilaginous border, and comprises a change of the normal lymphoid marrow, which is rich in cells, into a tissue poor in cellular elements, which contains but few blood vessels and consists of a homogeneous ground substance containing spindle and stellate cells. The transformation of the marrow with the associated destruction of osteoblasts, while normal bone absorption proceeds, must necessarily result in an abnormal thinness and insufficient density of the youngest portions of the diaphysis, at the margin of growth. From this circumstance a great rarefication of the bone results both in the region of the first lamellæ and in the deeper layers.

Consequently the ends of the shafts of the diseased bones become brittle on account of the thin cortex, the scarcity of strong trabeculæ and the persistence of much calcified ground substance which has not been transformed into true bone. On this account even small traumata, such as the traction of the muscles at their attachments, lead to partial or complete fractures at the extremities of the long bones and to displacement of the costal cartilages (see Plate 9). Breaks very rarely occur at a great distance from the epiphyses, as in the shafts. As a result of the fissures and fractures at the epiphyseal line, the epiphyses become loosened and dislocated but no true epiphyseal separation occurs. Severe displacement of the fragments is prevented by the fact that the periosteum is very seldom torn. The joints always remain unaffected.

Subperiosteal hæmorrhages of varying extent, surrounding the entire shaft, usually accompany the breaks in the bone and often lead to visible and palpable swelling of the limbs. These hæmorrhages,

however, may be absent notwithstanding severe bone lesions; they are dependent upon the severity of the hæmorrhagic diathesis which accompanies the bone affection. This leads to hæmorrhages, not only about the fractured bones but also on other bones, especially where growth is very active, *e.g.*, the jaws; also to hæmorrhages in the bone marrow, into the parenchyma of the internal organs, and into the intestinal mucosa (diffuse ecchymosis of the mucosa of the ileum, Fränkel). In several cases which had had hæmaturia Fränkel found no inflammatory changes in the kidneys but merely hæmorrhages into the tissue.

According to the same authority radiographs of the diseased bones show characteristic features; in the lower portions of the diaphyses, in place of the fine meshwork of the spongiosa there occurs a washed out space with irregular margins. If the case recovers this disappears only after some months. Breaks in continuity and subperiosteal hæmorrhages are easily recognized. (For a personal observation see Plate 10).

After the absorption of the necrotic material at the point of fracture (the "Trümmelfeld" zone of Fränkel) the regeneration of the bone takes place through the appearance of small masses of normal lymphoid marrow cells in the pathologically rarefied marrow, and the replacement or removal of the latter by their gradual growth. After that the formation of new bone proceeds normally and strong osseous trabeculæ are formed. If marked dislocation occurs after a fracture a deformity may remain in the neighborhood of the joint.

Relationship to Rachitis.—Schoedel and Nauwerk believe that rachitis plays a special rôle in infantile scurvy; on the other hand, Naegeli, Schmorl, Stooss and Fränkel consider them as independent affections, though they recognize their frequent association which may be explained by the children's age and the artificial feeding. Cases of infantile scurvy of the severest grade exist without a trace of rickets, and the anatomical changes in the two conditions are essentially different.

The question whether or not infantile scurvy is to be considered as scurvy cannot be decided until we possess satisfactory reports upon the histology of the bone changes in the latter disease. The macroscopic lesions seem to be very similar (Netter, Stooss). At all events, clinically, infantile scurvy and scurvy are closely related and the majority of physicians are inclined to regard the two diseases as practically one. From a scientific standpoint the decision will first be made when the above-named condition is fulfilled.

Etiology.—The specific cause of infantile scurvy is as yet unknown. Two factors play the principal rôles in its causation: (1) the kind of food the child has had and (2) a special individual susceptibility.

Only artificially fed children are affected, and the unsuitable diet, which, considering the needs of the child, is insufficient, must have been maintained for several months. Whether breast-fed children can be

affected is doubtful; the few cases of this kind reported in the literature are not free from criticism. As severe a grade of malnutrition can occur with mother's milk as with artificial feeding when the breast-milk does not supply the special needs of the suckling (autointoxication, Variot).

The loss of certain fresh properties in the milk, through heating it, is one of the most important causes of this affection, and other important factors are insufficient feeding and monotony in diet.

Individual predisposition is shown by the fact that of twins who have had the same nourishment one may thrive splendidly and the other become affected. Finkelstein saw an infant ill with the disease who, because a brother had formerly suffered with the same complaint, had received only milk heated for a short time, and fresh vegetables.

Infantile scurvy occurs with all forms of artificial feeding but certain methods favor its appearance. Sterilized and prepared milk of various sorts come first, then pasteurized milk and simple boiled milk, then milk and flour mixtures and prepared flour alone, and finally oatmeal gruel and rice gruel. With the use of raw cow's milk the disease is rather rare.

The manifold attempts to give to cow's milk a "human character," the undue valuation of its special natural properties and the over valuation of the modification of its gross composition to as near as possible that of human milk, have all favored the increased occurrence of this formerly almost unknown disease. The more frequent occurrence of the affection in the families of the rich than in those of the poor is explained by the fact that specially prepared milk and the many proprietary foods are, on account of their high price, more accessible to the well-to-do than to those in less easy circumstances. Besides this, an undesirable uniformity of food is not infrequent in the diet lists of well-to-do families.

One should be prepared to meet infantile scurvy everywhere, among poor and rich alike. Cheadle noted the relative immunity of the children of the poor, and ascribed this fact to the circumstance that early in life these children subsist on fresh food added to their milk. In cases of this kind continued underfeeding with oatmeal gruel, rice gruel, etc., has sometimes taken place, but in general the caloric value of the food which preceded the appearance of infantile scurvy has been more nearly sufficient.

Among the unavoidable changes which take place in milk when it is heated, and which have been considered as etiological factors in infantile scurvy are: (1) the destruction of a certain amount of nucleon-phosphorus; (2) the destruction of all enzymes; (3) the change of soluble calcium compounds into insoluble calcium phosphate; (4) the conversion of a certain amount of the amorphous neutral calcium citrate into the less soluble crystalline form. Netter considers citric acid as the specific

antiscorbutic constituent of cow's milk, but as the latter is much richer in citric acid than is mother's milk, a deficit cannot easily occur even with cooking.

Johannessen, in conformity with the recent theory that marine scurvy is due to an intoxication, suggests that toxins from the killed bacteria in the milk may have a part in the production of infantile scurvy. Neumann seeks the cause in a chronic poisoning: "The poison may arise exogenously from the food by bacterial action, by chemical means or by the action of heat, or it may arise endogenously during digestion." In the conclusions which are drawn from the collective studies of the question by the American Pediatric Society the possibility of an autointoxication is suggested. The supposition that infantile scurvy is due to some toxin arising in the food and that this affects only certain susceptible children while the great majority thrive on the same nourishment would most easily explain the whole symptom-complex, and the prompt action of dietetic therapy, the result of a simple change in diet.

Microscopic examination of the blood and other tissues, and special bacteriological experiments (Schmorl) have so far given no support to the theory of a direct bacterial origin of the disease, nor have any results been derived from its attempted artificial production in animals (Bartenstein).

Diagnosis.—If one carefully considers the symptoms which have already been described, this disease will hardly be mistaken for any other, but it is of great importance to make the diagnosis before the disease gains much headway. If in a bottle-fed infant a progressively severe anæmia develops with a coexistent suspicion of hæmorrhagic swelling of the gums, and tenderness at the epiphyseal ends of the long bones one should think of Barlow's disease—infantile scurvy.

Mistakes frequently occur through the observation of marked unilateral swellings on the long bones; the diagnosis of periostitis, ostitis, osteomyelitis, osteosarcoma, etc., is made, even operations of greater or less magnitude are undertaken without result, until the death of the child or the discovery of subperiosteal hæmorrhages puts one on the right track. The entire clinical picture should not be neglected, the severe anæmia, and its gradual development should be sufficiently appreciated; the entire child should be examined.

In contrast to severe anæmias from other causes with a tendency to the occurrence of hæmorrhages, it is important to remember that aside from a considerable reduction in the percentage of hæmoglobin the blood changes in infantile scurvy are not characteristic (see above).

Infantile scurvy is readily hidden behind an associated rachitis, or may be mistaken for rachitis, though the latter does not exist at the time. For this reason the progressive anæmia, the affection of the gums, and the painful swellings on the long bones are all very impor-

tant. Swelling and sensitiveness at the osteocartilaginous border of the ribs is common to both diseases; an angular fracture between the prominent bony part and the depressed cartilage, or possibly even a depression of the sternum together with the cartilaginous portion of the ribs speaks for infantile scurvy. In congenital syphilis swellings similar to those of infantile scurvy appear on the long bones, and the condition of pseudoparalysis is frequent in congenital syphilis, marked anæmia also occurs, but in addition there are the other usual symptoms of syphilis. The peculiar gingivitis and eventually the other signs of the hæmorrhagic diathesis are very valuable. Radiographs of the diseased bones can be of especial service in difficult cases.

Incipient and abortive examples of infantile scurvy make themselves evident by the increasing anæmia, the restlessness and the hyperæsthesia of the children.

Prognosis.—In simple cases the prognosis is favorable if the diagnosis is made and dietetic therapy instituted; but if a complicating intestinal catarrh or bronchopneumonia exists, or if the cardiac strength of the child has already seriously suffered, the prognosis is doubtful in spite of proper feeding.

The mortality is still high, as the diagnosis is often not made, though it is to be hoped that with increasing knowledge of the characteristic symptoms, the ability to make the diagnosis will be improved, and with this the prognosis.

Prophylaxis.—If a marked anæmia develops with artificial feeding it is advisable, in order to rectify the diet, to give fresh food occasionally. Sterilized or prepared milk should not be given over a long period of time without the addition of fresh fruit or vegetables; and in general fresh briefly boiled milk should be used. Uniformity of diet for many months should be avoided and malnutrition corrected as soon as possible.

Treatment.—The treatment of this disease is generally as easy as it is satisfactory. A proper change in diet, without the help of any medication, leads in a short time, even quicker than in ordinary scurvy, to a complete revolution in the objective and subjective condition of the patient. Severe conditions and menacing appearances diminish in an almost magical manner. In place of the food which has heretofore been given, the child should receive fresh, at most briefly heated, or still better raw, cow's milk, if such is to be had from a reliable source. Besides this two to four teaspoonfuls per day of raw meat juice should be given, and the same amount of fresh fruit juice (obtained according to the season of the year from oranges, grapes, lemons, cherries, currants, blackberries, apples, pears, apricots, huckleberries, etc.) sweetened with sugar.

To children in the second or third years one can give in addition to the fresh milk, potato, vegetable soup (carrots, cabbage, cauliflower,

PLATE 10.

I

II

I. Upper extremities and pelvis of a 12-months infant with typical infantile scurvy.
II. Left arm of the same case.

spinach), stewed fruit, green salads, and finally chopped meat. The food is usually taken eagerly. After one or two weeks the symptoms will for the most part have disappeared. If gastric or intestinal catarrh exists one may give briefly-boiled milk with oatmeal gruel, currant, blackberry or elderberry juice, chicken jelly, or better still, breast-milk, even to children over one year of age.

The tenderness of the limbs, the fractures, etc., demand rest, avoidance of all unnecessary handling, and local applications. The complete repair of the bone lesions may be delayed for several months.

RACHITIS

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Occurrence.—Rachitis is an extraordinarily wide-spread disease. It occurs most frequently in the civilized portions of the north temperate zone, where in the poorer quarters of great cities it affects 90 or more per cent. of all children. It is comparatively infrequent in the tropics on the one hand and in the far north on the other and also at high altitudes. It is very rare among the children of the yellow races, but although negro children in the tropics remain practically exempt those in regions in which it is endemic seldom escape.

Symptoms.—The most characteristic symptoms of rachitis are those of the osseous system; in addition to these certain general manifestations which are apt to be most evident occur in the majority of cases at the beginning of the disease at a time when the bony changes are not yet clinically evident.

(*a*) *Constitutional Symptoms.*—These are quite ambiguous. The children become restless, ill-tempered and do not sleep as well as usual. If they lie on their back, especially in sleep, they roll their heads from side to side or burrow them into the pillow, though if they lie on the side they usually remain quiet. Children over six months of age with this disease learn to seek the latter position of their own accord, not infrequently gradually lying even partially or wholly on their faces. When such a child is carried it is unable to hold its head erect for more than a short period of time, and usually supports its cheek or face against the face or shoulder of the nurse. Oftentimes the friction of the head on the pillow leads to baldness of the occiput.

Another important symptom is *sweating*. This affects the head, principally, where it is often so marked that in the morning the child's pillow is soaked through. The sweat is of a clammy nature, with an acid odor and reaction. Oftentimes sudamina or eczema follow in the wake of the excessive sweating. Coincidentally the vasomotor excitability of the skin undergoes an abnormal increase, so that red spots appear in a short time over any area where friction is exerted. Very frequently the urine assumes an offensive penetrating odor. In children old enough to run about the absence of desire to do so is often a very early symptom of the disease.

If these initial symptoms are very marked the children lose their

fresh appearance and become more or less pale and flabby. In many cases the constitutional symptoms are so slight that the disease begins apparently with those referable to the bones, though the former are usually manifest at least two or three weeks before the undoubted bony changes are evident.

(*b*) *Osseous System.*—The bone changes due to rachitis may be comprised in the terms "softening" and "deformity." The softening affects principally the flat bones and the diaphyses of the long bones, but the deformity may affect any bony part. They are constant even in cases in which gross deformity never appears. As the result of the disturbance of the bony growth the epiphyses of the long bones enlarge, especially at the points of union between the bony and cartilaginous ribs where they can become so marked that they appear as large nodules lying under the skin. The skin not infrequently forms a deep fold in the plane of the articulation, especially at the wrists.

Fig. 32.

Rachitis. Three-year-old girl with rachitic rosary and gaseous distention of abdomen.

In the majority of the more chronic cases a deformity of the diaphyses is gradually superimposed upon the enlargement of the epiphyses. Such deformities frequently take the form of marked exaggeration of the normal bony curves, but the essential condition underlying these important changes of form is always some trauma which bends, or much more rarely fractures, the abnormally soft bones. Marked displacement of the fragments is usually absent, even with complete fractures, since the continuity of the thickened periosteum almost always remains intact. The consolidation of the callus is much delayed by rachitis. The force which is necessary to bend or break a rachitic bone is in inverse ratio to the extent of the bony softening. In the worst cases therefore very careful protection of

the child is necessary. Often in a very short time the bones become markedly softened, even under the eyes of the observer.

In cases of less marked bony softening, partial fractures can take place during powerful muscular contraction, as for example, in the forearm following tetanic or eclamptic convulsions.

In almost all cases in which the disease has lasted for a number of months the body length of rachitic children is less than the normal average for their age. In such cases the shortening of the bones is caused not only by the bowing but, at least in the more severe cases, by a true injury to the longitudinal growth especially in the bones of the lower extremities. In many cases there develops toward the end or after the cessation of the active stage, an almost complete absence of growth which leads to dwarfing.

An impairment of the motor functions usually coexists with this deformity of the skeleton. Only a minority of rachitic children learn to stand or walk at a period approaching the normal; with most of them the time is postponed for months or even years. Children that are walking at the onset of the disease quickly lose this function. In addition to the fact that rachitic children do not learn to stand or walk at the proper time, the majority of them use their legs very little or indeed not at all, and if one attempts to place them upon their feet their knees strike together. If the legs are not used at all they remain as a rule free from deformity, and in such cases the epiphyseal enlargement frequently does not occur. The upper extremities are remarkably spared in many children, but in very severe cases they too are very little used.

This disinclination to move is associated with a striking laxity of the voluntary muscles. The physiological tone is wanting in these cases, and as a result the limbs of such children can be easily placed in positions that are otherwise impossible except in the case of so-called "snake men" or sometimes in individuals with wide-spread atrophic paralysis. This muscular hypotonicity is greatly misinterpreted, and rachitic children are described as having an abnormal laxity of the periarticular ligaments. Hagenbach-Burkhardt refer to this abnormal hypotonicity as a specific (rachitic) weakness of the muscles but I am far more inclined to regard it as an interception of the innervation. In many cases the rachitic bones are distinctly sensitive to pressure, but even where this is not so, the muscular contractions can cause very severe bone pains, because at such time the tendons necessarily exert traction on the softened thickened periosteum, upon which they are inserted. It is very easy, therefore, to suppose that children learn to inhibit any nervous stimulus which might bring pain in its wake. In the later stages of the disease the deformities may mechanically render motion difficult.

Only in rare cases does faulty nutrition cause a backwardness in

learning to stand or walk. Often when rachitic children do finally learn to walk they have, in severe cases after a year or so, a waddling gait and become easily tired on account of the deformity of the pelvic girdle and of the lower extremities.

Rachitis very frequently leads to the following striking clinical changes on the part of individual portions of the skeleton.

A *disproportion between the face and head* often exists due to the fact that the growth of the facial bones is slower than that of the bones of the skull. This disproportion is especially striking in the case of older individuals. In rachitis the transverse diameter of the upper jaw is decreased but is definitely increased in the sagittal plane so that it projects forward in the mid-line like a beak. In contrast to this the under jaw is shortened in the sagittal plane; the physiological curve in the region of the incisor teeth is flattened, and the normal curve in the region of the canine teeth becomes angular. The lateral portions of the jaw converge, while its thicker lower edge turns upward and the alveolar margin bends inward. The incisor teeth are often bent sharply inward so that when the mouth is closed there remains a space of several millimetres between the lingual surface of the upper and the labial surface of the lower ones. The inner surface of the upper molars often rests against the outer surface of the lower molars. As a consequence of the lack of development of the alveolar process there not infrequently results a lack of sufficient space for the teeth.

Fig. 33.

Rachitic scoliosis. Three-year-old girl.

In almost all cases *dentition* is prolonged by rachitis; oftentimes children begin their second year with no teeth, although the termination of the first dentition in such children usually occurs in the third

year. A characteristic phenomenon is the cutting of many teeth in close succession after a considerable period of time. As a rule rachitic teeth are less resistant than normal ones, and the enamel often shows horizontal and longitudinal striations or roundish depressions. Frequently the teeth are discolored; they may be yellowish, brown, black or greenish gray. They are inclined to become carious and to fall out, or they gradually crumble down to the alveolar edge. Sometimes only the upper teeth behave in this manner while those in the lower jaw remain intact.

In the *cranium*, long standing rachitis leads to a thickening of the frontal and parietal tuberosities which, with marked prominence of the tubera frontalia and a simultaneous flattening of the occiput, gives a cubical or dice-like shape to the skull. These are cases of so-called "caput quadratum" or square head.

In rachitic children the large fontanelle often reaches an abnormal size, and is often closed only at the end of the second year or even later. The small fontanelle and the two posterior lateral fontanelles remain open in many cases an abnormally long time, as do the longitudinal, the coronal and the lambdoidal sutures. The bony edges of the large fontanelle are often so soft, either partially or throughout their whole extent, that they can be easily depressed. Often other places in the skull are soft and compressible. This so-called "*craniotabes*" occurs principally in the region of the lambdoidal suture and the small fontanelle; it may however extend far into the occipital bone or into the posterior part of the parietal bones. The soft areas are usually about the size of a dime but they not infrequently unite to form larger areas, and in the severest cases the softening affects almost the entire occiput. The latter is flattened in all severe cases. The temporal veins are frequently markedly dilated in severe cranial rachitis.

The rachitic spinal curvature as a rule does not form an angular projection but rather a more or less gentle bend. Most frequently one finds a kyphosis which, in typical cases, involves the lower dorsal and lumbar vertebræ. Next in frequency is the dextro-convex-dorsal scoliosis; as a rule a second curve is present compensatory to the first.

In the *thorax* the most constant symptom of rachitis is the occurrence of a row of bead-like enlargements which run from above anteriorly to below laterally at the junction of the bony and cartilaginous portions of the ribs, the so-called rachitic "rosary." These enlargements are more pronounced on the lower than on the upper ribs; that upon the 11th rib occurs normally in about the mid-axillary line. On closer examination each single nodule consists usually of two swellings separated by a furrow, one of which belongs to the osseous and the other to the cartilaginous part of the rib. In emaciated children the rosary is plainly visible but in fat or even well nourished individuals it can be demonstrated only by palpation.

Fig. 34.

Severe deformity of the thorax. a. posterior view. b. the right side. c. from below.

In the majority of severely affected children a still further malformation of the thorax is associated with the rosary. The most important visible evidence of this is the flattening of the lateral chest wall. This flattening is most marked as a rule between the mammary and postaxillary lines and between the 4th and 7th ribs. In severe cases, in place of the normal bowing of the lateral chest wall with the convexity outward, a more or less deep hollow is present, so that here the ribs describe a curve with a concavity outward. In contrast to the lateral

Fig. 35.

Deformity of the thorax, pelvis, and extremities.

wall of the chest the sternum in these cases usually projects forward, and if a kyphosis exists at the same time the sternum curves convexly forward from above downward. In rare cases the deformity does not assume the classical form of the rachitic "chicken breast," but with the typical flattening of the chest wall the sternum lies somewhat depressed between the very prominent costal cartilages. The posterior surface of the rachitic thorax is abnormally flattened and the borders between the posterior and lateral walls are usually prominent. In contrast to the flattening of the central portions of the chest wall, the lowest part

projects outward, the sharp transition from one to the other forming the so-called "Harrison's grooves" which run around the chest at the level of the diaphragm.

As a whole the chest appears strikingly small in its upper two-thirds, especially in comparison with the head and belly. The deformity of the thorax in rachitis is caused on the one hand by the abnormal weakness of the chest wall which yields in time to the diaphragmatic contractions at each inspiration and to the elastic pull by the collapsing lungs at expiration, and on the other to the continual pressure exerted by the overlying upper arms. The flattening of the posterior chest wall is the result of the continuous dorsal decubitus. The bulging of the costal margin is caused by the rachitic enlargement of the liver.

Fig. 36.

Bead-like fingers.

In this disease the normal curves of the clavicle are pathologically increased; frequently the clavicle is the seat of angular partial fractures which affect chiefly the middle anteriorly convex curve of the bone. The humerus is visibly curved only in severe cases; the convexity of the curve is as a rule outward and somewhat backward. The enlargement of the proximal epiphyses causes nothing special to be noted in the living child, but that of the distal ones is quite often easily palpable and in emaciated children is visible. The humerus frequently shows partial or complete fractures, usually about in the middle of its diaphysis, and later, a marked formation of callus. The length of the upper arms may be shortened as much as one-half, partly through inhibition of the longitudinal growth, partly through bending and angulation.

In the forearm, the enlargement of the epiphyses, especially the distal ones, is the most constant symptom. The diaphyses frequently show a convex curve, the most prominent part of which usually lies in the distal half of the forearm, and in addition a spiral bend of the radius about the ulna is often found which causes a more or less marked permanent pronation of the hand. The phalanges are frequently thickened and spindle-shaped, causing the fingers to assume the appearance of a string of beads.

Fig. 37.

Rachitic X-shaped legs.

Of the rachitic deformities of the infantile pelvis the thickening of the iliac crests has the greatest clinical interest. In the femur the distal epiphysis is often markedly thickened, and the bone is bent with the convexity as a rule forward or outward. Partial fractures are not infrequent here and usually occur in the middle of the diaphysis. In the bones of the lower leg the distal epiphyses as a rule enlarge more markedly than the proximal ones. Very often partial fractures are found here also, usually situated in the lower third with their convexity towards the front and outer side. Besides these fractures an outward rotation of the entire leg occurs. These cases are often called "saber legs." If *genu varum* is added to this the so-called "O legs" are formed, the foot assuming on this account in some cases the varus and in others the valgus position. In "X legs" the valgus position exists in both the knee and ankle-joints. In the so-called "baker's legs" one of the extremities assumes the valgus position while the other remains almost straight. In rare cases *genu varum* is found on one side and *genu valgum* on the other. In their longitudinal growth the lower extremities are more frequently adversely influenced by rachitis than are the upper.

The osseous deformities of rachitis appear in a very definite sequence as to time. Only in exceptional cases can distinct clinical symptoms

referable to the bones be noted before the end of the third month. Until about the seventh month one finds chiefly craniotabes and the "rachitic rosary," which corresponds to the more marked growth of the skull and thorax at this time. During the second half year craniotabes very frequently increases in extent and intensity. It is especially at this time that thoracic rachitis becomes prominent. The ribs become weak, the rosary often becomes very marked, and the deformity of the thorax begins. Towards the end of the first year we not infrequently find the kyphosis. If the disease begins after the end of the first year craniotabes usually does not occur. The thoracic changes still appear, but at this time the deformities of the extremities are most marked. In addition kyphosis and scoliosis are seen, and, as a late form of the cranial rachitis, the bulging of the frontal and parietal eminences. The deformities of the extremities are especially marked in those cases in which the children run about in spite of the rachitis. Permanent deformities first appear as a rule towards the end of the second year.

In cases in which rachitis begins in the middle of the first year, and remains active far into the second year, the three different stages can be seen in the same child. They pass from one to another in sequence without sharp demarcation. In such cases the craniotabes usually begins to diminsh at about the end of the first year, or indeed even earlier, while the disease advances in other parts. While the clinical symptoms referable to the skeleton are gradually developing, the constitutional symptoms, with which the disease began, usually persist. In a large number of cases all the deformities undergo complete resolution after the active disease is cured, but in very severe cases disfiguring secondary deformities remain throughout life. The marked angulations which result from faulty union and consolidation of the diseased bones are not capable of complete resolution. Of the greatest importance are those cases in which kyphoscoliosis remains, or in women, well marked pelvic deformities. In less unfavorable cases the after effects consist merely of irregularities of the bony structures, of remains of the "chicken breast" and of anomalies in the position of the teeth. In the mildest of the severe cases one finds in adults, aside from erosions of the teeth, merely an eversion of the costal arch with the presence of Harrison's grooves.

(*c*) *Other Organs.*—A very small number of cases of rachitis present a generally excellent condition of nutrition and a rosy clear complexion. This is especially true in breast-fed children that are only slightly rachitic. The majority of children, although they may have been thriving before the beginning of the disease cease to gain in weight at its onset, and their body weight then remains more or less below the normal throughout the course of the affection. Coincidentally the skin becomes pale and flabby and not infrequently assumes a dirty grayish yellow cachectic hue. The examination of the blood has so far given no

characteristic results. Elevations of temperature which are observed in rachitis are always seen at the onset of complications.

The mental development is usually not retarded, except in very severe cases in which the general condition is much depressed, and also in those children who by being unable to run about and play are prevented from learning from other children. The typical disposition of rachitic children, although it is by no means marked in all cases, is one of irritable ill-temper. In protracted cases with bone pains the children finally greet every one coming near them with piercing cries; moderate cases usually show evidence of pain only when handled.

The muscles, especially of the lower extremities, may become extraordinarily atrophied in those severe cases in which the children for a long time shun all movement, but the normal electrical excitability always remains. In consequence of the fact that the thoracic muscles are involved in the general muscular weakness the respirations are mainly diaphragmatic. Continued rapid breathing, frequently with dilatation of the nostrils occurs in all cases of extreme thoracic rachitis, although no complication may be present in the lungs or bronchi. Even with normal breathing every inspiration retracts the already flattened or even concave lateral chest walls.

The percussion note is deep and loud over the concave areas; over the prominent parts of the chest higher and shorter. With considerable thickening of the shoulder blades one can find almost absolute flatness in the supraspinous fossæ. The area of cardiac dulness may be increased in marked deformity of the chest even without cardiac hypertrophy and the heart shock can be felt beyond the usual boundaries. The respiratory murmur, provided no pulmonary complications exist, is loudest where the percussion note is fullest. In rachitis auscultation is of far more value than percussion for the establishment of a diagnosis of pulmonary disease. In doubtful cases it is always advisable to form one's final opinion only after many very careful examinations. The kyphoscoliotic bowing of the vertebral column causes further displacement of the organs and consequently leads to further errors in the usual topographical diagnosis. With a severe thoracic rachitis the pulse is usually quickened.

The appetite is frequently very good, particularly for sweet and starchy foods. The abdomen is almost always markedly distended with gas and therefore soft and not sensitive to pressure. The condition of the bowels is not at all characteristic. In many cases constipation exists and often the feces show a striking lack of the normal pigments. The liver may be depressed by marked thoracic deformity and may, upon superficial examination, appear to be enlarged although in reality it is only dislocated downward; with severe rachitis occurring in anæmic children in poor condition it is often truly hypertrophied. A marked

enlargement of the spleen is rather rare, and only occurs when a high grade anæmia exists. In many of these cases one has to deal with a complicating hereditary syphilis. The swelling of the lymph-nodes, which is frequently noted, has nothing to do with rachitis *per se* but is always an evidence of complications.

Time of Onset, Duration and Course.—A positive case of congenital rachitis has as yet not been observed. The so-called fœtal rachitis has no connection with true rachitis. In the great majority of cases the first clinical symptoms in the bones are noted only after the third month, as a rule even in the second half year. After the beginning of the second year the number of recent cases diminishes, and the disease only exceptionally develops after the end of the second year.

It usually lasts for several months; often more than a year, sometimes more than two years. An acute form of rachitis is not recognized. Very frequently in an individual case certain of the very numerous clinical symptoms are absent, and at any stage of the disease its development may cease; especially is this true of craniotabes which often heals without the development of any further rachitic symptoms. The first evidence of a beginning recovery is a lessening of the general symptoms. In very severe and prolonged cases the children may remain weakly for at least a year after the final cessation of the rachitic process.

Complications.—The laxity of the abdominal wall and the atony of the intestinal musculature, which is encountered so frequently in this disease, give rise to a tendency to the occurrence of umbilical herniæ. These herniæ usually remain small but they can, especially under the influence of an intercurrent whooping-cough, attain to the size of plums or even larger. Their prognosis is always favorable.

Complicating pulmonary diseases arise very easily with severe thoracic rachitis. Even a moderate bronchitis can be dangerous to life in this condition. A prognosis should therefore always be made with care. The worst feature is the fact that, in rachitis, catarrh has a dangerous tendency to descend to the finer bronchioles, especially in poorly nourished individuals, and thus to lead to capillary bronchitis and bronchopneumonia. The prognosis for the last two diseases is always grave in rachitic children.

Diseases of the gastro-intestinal canal are frequent and serious complications. Especially to be feared are those catarrhal diseases of the large intestine which are accompanied with mucus stools. In the case of debilitated children the associated intestinal catarrh frequently becomes the specific cause of death.

The nervous complications are very important, especially spasm of the glottis, eclampsia and tetany. The importance of these spasms lies in the danger of sudden death in a laryngospastic or eclamptic attack. Sometimes nystagmus, rotatory spasm or spasmus nutans

occur. The prognosis of these forms of spasm is good, and recovery almost always ensues after a few months of antirachitic treatment. The occasional occurrence of cataleptic conditions in poorly nourished rachitic children should be noted. The symptoms are those of the well marked "*Flexibilitas cerea.*" Finally, the fact can hardly be disputed, that children with severe rachitis are more disposed than others to tuberculosis of the various organs.

Pathological Anatomy.—According to the severity of rachitis, the anatomical changes are of vastly different grades, from the very light manifestations, whose differentiation from physiological states is difficult, to the severest lesions. In all cases except the mildest the rigidity of the bones is markedly impaired; occasionally this advances so far that one can bend the bones as if they were made of rubber. At the same time there exists a considerable hyperæmia of the periosteum and marrow. The periosteum is more or less, often very markedly, thickened; the thickening being due almost entirely to an increase of the cambium layer. Directly under the fibrous layer are found uncalcified spicules of young bony tissue formed by ossification of the periosteum; between them lie the primary periosteal marrow spaces. In the deeper layers of the swollen cambium the new formed bony spicules are stronger, and the spaces between them are narrower. The spicules which were first formed contain calcified fragments in their central portions but consist otherwise almost entirely of uncalcified osteoid tissue. Further on one comes to the cortex proper into which open narrower vessel canals than the normal canaliculi. The lamellæ of the cortex everywhere show abnormally broad osteoid borders. Only in the places where the bony tissue is undergoing absorption, which is especially apt to be of greater extent in the neighborhood of the central marrow cavity, does the calcified bony tissue, which is well supplied with lacunar spaces, border directly upon the marrow tissue.

Fractures occur most easily at the time at which the new and proportionately soft deposits form a fairly thick layer upon the deeper, compact, and relatively thin bony sheath which surrounds the central marrow cavity. The breaks in continuity occur for the most part only in the compact layer while the young superficial layers are compressed. Breaks occur usually only in the concave portions which lie in the angle of fracture, similar to the breaks which occur during the forcible bending of a willow twig (green-stick fracture), or a feather quill. The fragments are displaced towards the convex side which narrows and often entirely closes the marrow canal; the marrow is accordingly pressed out and in part destroyed.

Callus formation occurs in every place where the bone is fractured and usually, too, for a considerable distance about the break. Sometimes the entire angle of fracture is filled with callus which usually

forces itself into the marrow cavity through the aperture of the fracture and thus leads to a complete closure of the cavity at this point. A continuous marrow cavity is reformed only a very long time after consolidation. Rachitic callus bears a close resemblance to the young periosteal growth except that it far more frequently contains true cartilage.

In the lightest cases the periosteal thickening affects only the edges

Fig. 38.

Longitudinal section through the proximal epiphyseal end of the tibia. Nineteen months old boy with moderately severe rachitis.

of the cranial bones, but in the more severe ones the tuberosities also are involved. The inner surface of the bones at all times remains free from rachitic deposits. The membranes which cover the sutures and fontanelles are lax, and thickened. The cranial bones are never all equally affected by rachitis; in typical cases the frontal bones are only slightly thickened at the edges, while the parietal bones are partly, and the occipital almost entirely, covered by a red spongy deposit. Very

frequently there occurs at the same time in the region of the occiput a thinning of the bony plates which in severe cases amounts to the appearance of membranous gaps. Such a membranous area always corresponds with a digitate (Pacchionian) depression of the inner surface, while on the outer side its upper surface lies on the same level as the surrounding tissue. In all these cases of craniotabes, the other bones, especially frequently the ribs, show macroscopic rachitic changes, and with microscopic examination one never fails to find osteoid tissue in these craniotabetic areas. As to the remaining flat bones, the only point to be emphasized here is the fact that the pelvic bones very early undergo the well-known changes which are so important in obstetrics; but apparently in the pelvis as well as elsewhere the rachitic lesions are in many cases either completely or partially resolved in the course of further growth.

The disturbances which endochondral ossification undergoes in rachitis are very characteristic. As a result of the delay in the ossification caused by the advancing growth of the cartilage cells, the primary growing margin assumes an abnormal width. Later on provisional cartilaginous calcification occurs but still only in an incomplete manner; then, through further cartilaginous growth, the formation of the marrow cavity advances irregularly over the line of ossification, and finally, by a continuation of the above phenomena, narrow marrow cavities are formed in the cartilage, the edges of which undergo a metaplasia into osteoid tissue. In all stages the newly formed bony tissue remains more or less completely uncalcified in the neighborhood of the line of ossification as it does elsewhere in the skeleton. With a continuation of the disease these phenomena always become more striking.

Very frequently the rachitic bones show a more or less marked degree of osteoporosis, in addition to the changes which have been above described. The consistency of the bones is probably impaired rather by a marked osteoporosis than by the persistence of the newly formed bone substance in an osteoid condition. After the complete cessation of the rachitic process the bones attain an abnormal thickness with a correspondingly increased hardness, and since they are thicker than normal there results a considerable increase in their weight. The apophyses and the other muscle attachments are unusually strongly marked, the normally sharp edges are rounded off, and their whole appearance is coarse and unsymmetrical. The erosions on the teeth remain throughout life.

Of the lesions in the soft tissues only the rather frequent occurrence of extensive enlargements of the ventricles of the brain needs mention.

Pathological Chemistry.—The water content of rachitic bones is higher than normal; in the fat content there are no constant differences. The most important chemical property of rachitic bones is the decrease

of mineral constituents, especially calcium and phosphoric acid. The percentage of ash in the ribs and vertebræ is especially low, often only 25 per cent., or less, of the normal. The specific gravity of the cartilages and the bones is decreased and the relative weight of the cortex of the spongiosa and of the cartilages is changed in favor of the cartilage. The soft tissues of rachitic children contain no less calcium than normal. The urine is usually faintly acid; during the active stage of the disease its calcium content is usually somewhat reduced while the percentage of calcium in the feces at this time is always slightly increased.

Relation of Rachitis to Osteomalacia; Late Rachitis.—The causes of rachitis and of osteomalacia are without doubt distinct. The patholog-

Fig. 39.

Osteomalacia.

ical processes in the bone are, however, in a manner the same. In osteomalacia the disturbance of endochondral ossification is less marked than the occurrence of osteoporosis, but this difference is explained by the diversity in the ages of the patients. The marked osteoid deposits in the bones in osteomalacia consist of new formed uncalcified bone tissue; in rachitis, on the contrary, there occurs in restricted areas supplementary decalcification of already normally calcified bone. Osteomalacia, therefore, from a pathological,—not an etiological,—standpoint, may be considered as a rachitis of later life. The transition forms which occur in young adults, over the classification of which as rachitis or osteomalacia there has heretofore been much argument, present no difficul-

ties with this perception of their relation. In the cases which have been described as infantile osteomalacia, and which curiously always occurred in girls, rachitis resembles remarkedly in its skeletal phenomena the otherwise characteristic behavior of osteomalacia of later life. These cases of rachitis are in marked contrast to those in which disturbances of cartilaginous ossification are the most prominent manifestations of the disease (von Recklinghausen's "pure rachitis").

According to the opinion of authoritative surgeons the static deformities which appear at the time of puberty develop upon the foundation of true rachitis. There are in such cases specific rachitic changes in the epiphyseal cartilages, and to a greater or less extent, periosteal osteophytic formation is also found.

Etiology and Pathogenesis.—The cause of rachitis is unknown. Siegert has again recently drawn emphatic attention to the occurrence of hereditary predisposition to the affection which, according to his theory, is transmitted principally by the mother. Children with this tendency are not protected by maternal nursing but in such cases the disease is usually mild. Only exceptionally does severe rachitis occur in breast-fed children. If this hereditary tendency is absent children often remain free from the disease even if fed artificially. Rachitis has no relation to hereditary syphilis.

Many explanations are offered for the nature and pathogenesis of rachitic bone processes. The decalcified remains of the new formed bone tissue finally reach the stage at which they are unable to absorb the lime salts that are abundantly present for their use. Only in this one respect is the calcium metabolism disturbed by rachitis; beyond a certain point the question is as little one of deficient calcium supply as it is of deficient calcium absorption.

It is true that if an experimental diet very poor in calcium is given to quickly growing young animals, it leads to a disease which seems, upon superficial examination, to be extraordinarily similar to rachitis. Histological examination, however, shows that here we have to deal not with true rachitis, but with an osteoporosis with rachitic-like changes in the periosteum and in the growing cartilages. With this pseudorachitic osteoporosis, in contrast to rachitis, the soft tissues also take part in the calcium deficiency. Furthermore Pfaundler has very recently proved in a brilliant manner that rachitic osteoid tissue is not able to correct its calcium deficiency by means of absorption from a solution of calcium chloride, but that in the pseudorachitic osteoporosis of animals fed with a diet deficient in calcium the calcium absorption is markedly increased.

Rachitis can also be experimentally produced by the feeding of acids in the same way as with a diet deficient in calcium.

The hypotheses according to which rachitis is due to a lessening of

the alkalinity of the blood, to the accumulation of lactic acid in the organism, or to the retention of abnormally large amounts of carbonic acid, are as equally erroneous as the one last considered, which assumes a primary disturbance in the calcium metabolism.

In the majority of cases rachitis develops in the colder part of the year in which the children very seldom go out of doors, just as it never occurs in wild animals in their free state, and very seldom in pastured animals, but very frequently in animals in stables and zoological gardens. Perhaps further investigations into these observations may some day lead to the elucidation of the origin of this curious disease.

Diagnosis.—Before the appearance of the characteristic skeletal changes the diagnosis of rachitis can be only presumptively made. In the newborn there occurs not infrequently a defective ossification of the flat cranial bones which can be confused with craniotabes, but it may be distinguished from the latter by the less marked limitation of the depressible areas to the occipital bones, as well as by its course, as it reaches its full development in the first week or month after birth, while true craniotabes never occurs congenitally and usually appears first after the end of the third month of life. Furthermore, according to the investigations of Friedleben, there exists in all children during the second three months of life a physiological increase of the bony absorption in the flat cranial bones which can be the more easily mistaken for craniotabes as it affects principally the posterior part of the skull. It is more frequent in artificially fed children than in those fed from the breast, and is clinically manifested by the fact that the posterior part of the cranial vault becomes flexible and compressible; on careful palpation, however, one always finds a feeling of complete elasticity of the bony plates while in rachitic craniotabes the affected areas have more or less completely lost their elasticity; they are not flexible but soft. Without other symptoms a diagnosis of rachitis cannot be made from the time of the appearance of the first teeth, for in non-rachitic children they often appear first in the 9th or even in the 11th month.

The softening of the thorax is shown by the retraction at each inspiration, and is most distinct with quiet breathing, but one should remember that in young children without rachitis the thorax is far more elastic than in later years, and that a corresponding suggestion of inspiratory retraction occurs even in absolutely normal infants. For an early diagnosis the occurrence of the rachitic rosary is far more important than the pliability of the thorax. Still it is to be emphasized that slight swelling at the costal end of the costal cartilages is frequently present even without rachitis. Naturally no sharp distinction can be made between these slight enlargements and the somewhat larger ones which are referable to rachitis. The same thing holds good for the

epiphyses of the long bones; here too there is a gradual transition between the pathological and physiological enlargements.

The early differentiation of rachitis from infantile myxœdema is very important. Myxœdematous children also present swellings on the costal cartilages and thickenings of the epiphyses of the long bones, and with them even more than in rachitis there is a delay in the appearance of the teeth, as well as in the closure of the larger fontanelle, and in learning to stand and walk. Nevertheless such a striking clinical picture is presented by the combination of a marked delay in the growth, with a considerable retardation of the psychic development, cretinoid physiognomy, a myxœdematous condition of the subcutaneous fatty tissue, and with macroglossia, that an experienced individual can easily make a correct diagnosis at the first glance even in the less marked cases. Furthermore in rachitis the skin is soft and delicate; in myxœdema it is dry and hard, often with much thickened epidermis, especially of the toes; the hair in rachitis is thin and soft, in myxœdema coarse and brittle; most rachitic children sweat a great deal, while as a rule myxœdematous ones do not; finally the poor appetite and extreme constipation of myxœdema are features which never occur in rachitis in such marked degree.

The confusion of infantile scurvy (Barlow's disease) and rachitis arises from the fact that the former malady was earlier considered to be the same as acute or hæmorrhagic rachitis. For the establishment of a correct diagnosis it should be noted that infantile scurvy preferably affects rachitic children, and that the occurrence of undoubted rachitic symptoms in no way excludes or modifies those of the other disease. Properly speaking the two diseases have only one symptom in common, namely the tenderness of the bones, and even this, especially in the legs, is apt to be of such extraordinary severity in infantile scurvy as is only very seldom seen in rachitis. The swellings on the bones in infantile scurvy, which are caused by subperiosteal hæmatomata, are easily differentiated from the epiphyseal enlargements of rachitis by their localization, as they affect not the epiphyses themselves but the neighboring portion of the diaphyses. There is moreover in the symptomatology of rachitis nothing which one could at all confuse with the other symptoms of infantile scurvy, namely, the affection of the gums, and the hæmorrhages into the eyelids and orbits, as well as the other indications of the hæmorrhagic diathesis.

Hereditary syphilis can enter into the differential diagnosis of rachitis in manifold ways. Among others the syphilitic pseudoparalysis of Parrot is confused with it, but the localization of the bony enlargements differs in the two diseases. In rachitis the swelling preferably affects the epiphyses; in syphilitic pseudoparalysis there occurs either a thick ridge which surrounds the bone just at the epiphyseal margin,

or a spindle-like swelling which involves both the epiphysis and the end of the diaphysis. A further differential point is the complete flaccid pseudoparalysis which gives the disease its name, and which often remains a prominent symptom, during the entire course of the affection. The pseudoparalysis affects the lower epiphysis of the humerus with special predilection; still this point should not be very much emphasized, as the distal epiphysis of the radius and indeed the bones of the lower extremities are often involved. More important is the fact that the syphilitic paralysis is very often unilateral or at least is more pronounced on one side, while the epiphyseal enlargements due to rachitis are almost always completely symmetrical; and in further contrast to rachitis the pseudoparalysis affects only one joint or at most a few. Lastly the time of onset of the swelling is very important. The pseudoparalysis is a disease mostly of the first three months of life while the epiphyseal enlargement of rachitis usually occurs at a later time. In rare cases the tibial deformity due to rachitis resembles the "sabre blade" form which is characteristic of syphilis, but usually the laterally bent rachitic tibia can be differentiated at the first glance from that due to syphilis, which is laterally compressed and bent directly forward. In the rare doubtful cases the rachitic origin of the deformity is improbable if no such marked deformities are found elsewhere in the body. Furthermore it should be again emphasized that a combination of rachitis and syphilis is possible.

A marked rachitic prominence of the frontal and parietal tuberosities can so strikingly exceed the facial portion of the skull as to suggest the occurrence of hydrocephalus, but in the latter condition the abnormal expansion affects the entire skull more symmetrically, especially the lateral areas lying below the tubera. Besides this the bulging and tension of the large fontanelle and the separation of the sutures are important symptoms. The position of the eyeballs in hydrocephalus is absolutely characteristic; they are rotated downward so that the lower and not the upper part of the iris is hidden beneath the eyelid and between the upper margin of the iris and the upper eyelid a strip of sclera is frequently visible.

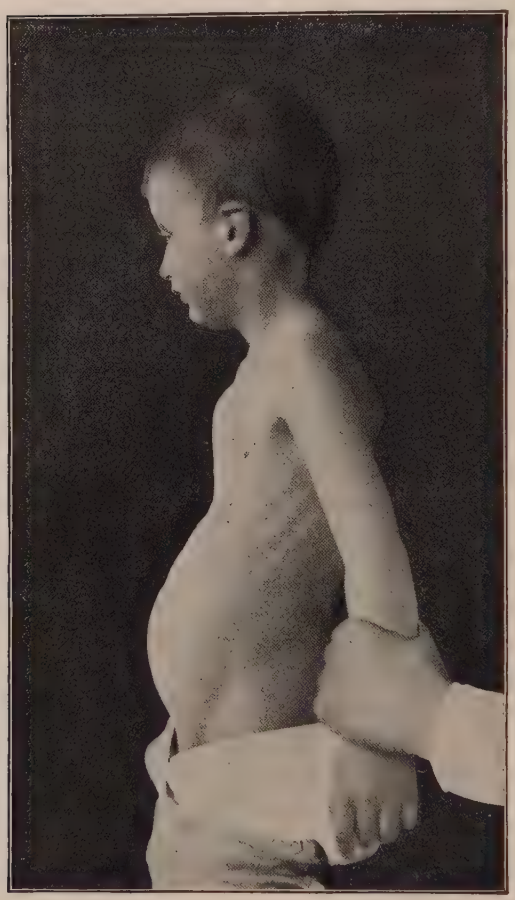
The differentiation may be very difficult if hydrocephalus begins to develop in a rachitic child. Often in such circumstances only the further course of the disease can bring a sure diagnosis.

The sharply localized tuberculous kyphosis which cannot be reduced without the use of force may be in almost all cases very easily differentiated from the like deformity due to rachitis, as the latter always involves many vertebræ, in a gentle curve rather than an acute angle, and can be partially or entirely reduced by raising the patient's legs when he lies in a prone position. The congenital "Trichterbrust," or Funnel Chest, differentiates itself from the similar deformity due to

rachitis by the tremendous retraction of the inferior end of the sternum. Rachitic coxa vara can simulate congenital dislocation of the hip by the high position of the trochanter major, and by the waddling gait. Other marked rachitis deformities usually point at once to the right diagnosis and in doubtful cases radioscopy throws a deciding light upon the subject.

As for the erosions of the teeth, the Hutchinsonian semilunar defects of the edges and the rounding off of the corners of the upper central incisors, while at the same time these teeth are shortened and diminished in size and are so placed that the cutting edges converge, must always, even in the slight cases, arouse a very strong suspicion of hereditary syphilis. The other forms of erosions so far as they affect the incisors and the first molars are due to a long standing rachitis.

Fig. 40.



Rachitic funnel-chest.

Frequently such a high grade of atrophy, flaccidity and inactivity of the musculature, especially of the lower extremities, is met with, that it is not possible, without other symptoms, to exclude with certainty a paralysis due to anterior poliomyelitis. In such cases an examination of the electrical reactions of the affected muscle-groups is necessary.

In especially marked rachitic meteorism with distention of the abdomen the differentiation from tuberculous peritonitis may be very difficult if the child is elsewhere possibly tuberculous; for indistinct dulness may be present in the dependent portions of the abdomen in both diseases, and the bowel movements may present the same greasy consistence, the same striking light color and the same very intense odor. In such cases, especially in the absence of fever, the examination of the urine for the diazo reaction is of value. In other cases the differentiation between the conditions mentioned can be safely made only after long observation.

Prognosis.—The light and medium cases of rachitis all progress to complete recovery provided they remain free from serious complications, and fall soon enough into expert hands for treatment. The warmer part of the year is more suitable for recovery from rachitis than the cold. The majority of the severe deformities disappear gradually during childhood; only in very severe cases do considerable disfigurements remain throughout life. In the most severe cases rachitic dwarfing may result. The danger of a persisting scoliosis lies in the fact that static influences may increase the deformity even after the cessation of the active rachitic process. Malformations of the thorax and spine may lead in later years to cardiac insufficiency, and malformations of the pelvis to obstetrical difficulties.

Prophylaxis.—With our present knowledge rachitis cannot with surety be prevented; but careful dietetic management is very valuable and the earliest possible antirachitic treatment is very important. The disease seldom takes a severe hold upon breast-fed children who live in dry sunny rooms, who are much in the fresh air and are bathed frequently. With artificially fed children an important point is the prevention of overfeeding. Children with severe thoracic rachitis should be carefully protected from whooping-cough, measles and influenza. If severe softening of the bones exists, the occurrence of multiple fractures should be guarded against by encasing the limbs in stiff dressings.

Therapy.—The best therapeutic agent for rachitis, according to my opinion, is codliver oil with phosphorus. This always acts especially quickly upon the general symptoms and upon the dangerous spasm of the glottis, a feature which shows an extraordinary superiority and one which no other antirachitic remedy shares with it. It is best begun with the dose of ½ teaspoonful daily of the usual solution [phosphorus .01 Gm., codliver oil 100 Gm. [phosphorus gr. $\frac{1}{6}$ and codliver oil ℥iii] and gradually increased to ½ teaspoonful twice a day. With this method of exhibition it usually agrees well with the patient. Codliver oil without the phosphorus is also a valuable remedy. One begins by giving a scant teaspoonful increasing the dose gradually to about three teaspoonfuls daily. It is best taken at meal time because it is then acted upon by the richly secreted pancreatic juice at the same time with the other food.

The diet of rachitic children has to be watched carefully in order that overfeeding may be avoided. With artificial feeding it is advisable to add some fresh fruit and vegetables to the other food even from about the seventh month, and to give, in addition to the cow's milk, meat broth, yolk of egg, fresh scraped mutton, fresh vegetable purée, fresh fruit juice and the like. Naturally, all these articles are to be given only in small amounts, and only once a day. In order to increase the diet of thin rachitic children a small teaspoonful of malt extract may be given two or three times a day, either clear or stirred in the milk.

Salt baths for fat, pasty children act well, but with thin erythematous ones they do more harm than good. They should be given two or three times a week for about 10 minutes at a time at about 33° C. (93° F.), and containing 1 to 4 pounds ($\frac{1}{2}$ to 2 kilos) of sea salt to a bath.

Residence at the seashore is valuable as a climatic cure but for various reasons it is only exceptionally available. In cases in which there is no special tenderness it is advisable to employ regular bathing with alcoholic liquids, or gentle rubbing with aromatic liniments. After the decline of the active stage, massage properly carried out for a month or so acts very favorably upon the general health, the ability to walk, and even upon the growth.

The Epstein rocking chair is especially recommended for children with beginning spinal deformity. With severe craniotabes it is well to

FIG. 41.

Epstein rocking chair.

have the head of the child lie upon a soft ring or upon a horse hair pillow with a depression in the centre.

Angular deformities of the long bones are best corrected in the active stage of the disease, but it is far more judicious to delay the orthopedic treatment of rachitic deformities of the limbs until the sixth or seventh year. Very frequently even severe deformities correct themselves spontaneously before this time if the child grows strong. In the case of rachitic dwarfs a long continued and careful treatment with small doses of thyroid extract is beneficial, in addition to the massage. The treatment of rachitic fractures of the femur by vertical extension is to be condemned, for rachitic bones which are vertically suspended undergo an acute softening, the anatomical basis of which is an acute rachitic osteoporosis.

PLATE 11.

DOUBLE RACHITIC COXA VARA.
(4-year-old girl)

DIABETES MELLITUS

BY
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DIABETES MELLITUS was formerly regarded as a very rare disease in childhood. This belief is not entirely correct as a great number of cases of diabetes in childhood have been reported in the last ten years, due not to its increased frequency but to its better recognition. Most statistics show that from .5 to 1 per cent. of all cases of diabetes occur in the first ten years of life but my own records embracing 2000 patients give 2.5 per cent. for the first decade. The second half of this period is more affected than the first, although the earliest infancy is not entirely exempt from this disease. Many cases at this early age are probably undetected; indeed many a child whose death certificate has stated gastro-intestinal catarrh, atrophy, asthenia, may in truth have died from diabetes.

It is therefore not superfluous to advise that the examination of the urine even in the earliest childhood be not neglected. Whoever regularly examines the urine of young children, will often be astounded by the positive result of the test for sugar and will be alarmed if he is not cognizant of certain peculiarities in childhood. Small quantities of milk-sugar may appear in the urine of breast- and bottle-fed babies and especially when milk-sugar is added to the bottle milk in order to overcome constipation or to improve the nutrition. This alimentary lactosuria is naturally of no importance. Milk-sugar may be identified by the yellowish red or brownish precipitate in Rubner's copper test instead of the cherry red color due to grape-sugar. The fermentation test is negative when the urine has been previously sterilized by heat. The best method of determination is to inoculate the urine with a pure culture of saccharomyces apiculatus: if grape-sugar is present there is marked fermentation, which is absent with milk-sugar.

Young children show a much greater tendency to *transitory glycosuria* than do adults. In severe diphtheria and especially in pneumonia with high fever the ingestion of moderate quantities of carbohydrates may induce a glycosuria, a resulting condition which occurs also in adults much oftener than the text books indicate. This is also transitory and to be attributed to functional changes in the pancreas due to the intoxication. I have seen this tendency to glycosuria continue several days longer than the original disease and in one case for two weeks.

On account of the relative frequency of this undeniable transitory glycosuria in children, the diagnosis of diabetes should not be made on the first finding of sugar. R. Schmitz also emphasized this in his well known work.

The general etiology, the pathogenesis and metabolic changes which have aroused interest in the scientific investigations of diabetes must be sought for in treatises which consider the disease in adults and also in certain special works upon the subject. Nothing of sufficient importance could be said in a few words and this is not the proper place for a lengthy consideration of the subject. Only the characteristic conditions will be mentioned.

Etiology.—Diabetes in childhood attacks boys and girls with apparently equal frequency. Some statistics indicate a slight preponderance of the female sex while among adults almost twice as many men as women are affected. Heredity seems to me to be much less marked than in adults, although there are instances where it plays an important part. I have recorded the medical history of a family in which there was a mild case of diabetes in the first generation, three female members of the second generation developed the disease at middle life and two children of the third generation died from severe and rapid types of the disease.

It is a very common experience that cases of diabetes among children do not occur isolated in a family. Several members are usually affected, not at the same time but one after the other when they reach a definite age. This was true in more than one third of the fifty cases of diabetes in childhood treated by me. If the family history is closely investigated it is often found that the parents are blood-relatives or that in a previous generation the marriage of relatives occurred. This confirms the opinion based on other grounds that diabetes in children as well as in many of the cases in adult life must be regarded as an endogenous degenerative disease. The well-recognized frequency of diabetes in the Jewish race probably depends upon the insufficient admixture of different strains of blood. The Jewish race certainly shows a marked tendency to diabetes in childhood but not to my mind in the same degree as among the adults. Besides hereditary influences, trauma (concussion of the brain) is often mentioned as a cause of diabetes in children,—whether correctly seems to me certainly more doubtful than in adults.

This is to be especially emphasized as we must regard progressive diabetes in childhood as pancreatogenous with at least the same certainty as ordinary diabetes. The examination of the pancreas macroscopically and microscopically reveals so few anatomical changes that in many of the older autopsy records it was not deemed necessary to mention its condition. In the last two decades attention has been

directed to the pancreas. The small size and relaxed condition of that organ has been given as a frequent finding. I myself have noted the latter condition, although no changes were discovered in the islands of Langerhans. It is of interest and deserves further observation that some of the children treated by me for diabetes had syphilitic fathers and that that disease was not completely cured at the time of the procreation of the child. In such cases it is possible that there might be a functional weakness of the pancreas due to the syphilitic virus. I have thought of this only recently and cannot fortify it with any great amount of clinical material.

Symptoms.—Course of Disease.—From the writings upon diabetes in childhood, the impression is frequently gained that the onset of the disease is usually quite sudden and that the disease begins at once as a severe type of glycosuria. My experience does not agree with this opinion since in the majority of my little patients there were periods of months or even years during which the glycosuria was of a mild type and immediately modified by the exclusion or even moderate limitation of carbohydrates. This knowledge has been gained by the fact that the urine of small children is tested for sugar more frequently than formerly. Cases which are regarded as severe directly after the detection of the disease, have probably not been observed in the early stages. The passage from a mild form to a severe type is therefore apparently much more rapid in children than in adults. So long as the disease is mild, there is little evidence of illness. The thirst may betray it or the flecks of sugar on the underclothes may attract the mother's attention. Complications such as disorders of the skin, diseases of the eye, neuralgias, etc., which in adults so often give the first diagnostic hint are practically unknown in the diabetes of childhood. When the diet is regulated, the thirst disappears and the children develop satisfactorily in their physical and mental growth.

After months or years the tolerance for carbohydrates fails. This is often induced by some foolish lapse in diet or oftener by an intercurrent febrile disease (tonsillitis, diphtheria, pneumonia, influenza, etc.), which so often even in the diabetes of adults produces a rapidly incurable change. Even when such causes are absent the lessened tolerance is only postponed, not removed and the diminution quickly changes into complete loss. A period of a few months, often but several weeks may elapse between a tolerance for 80–100 grams of bread and the complete development of a severe type of glycosuria, no longer modified by the withdrawal of carbohydrates. As soon as the loss of tolerance appears, the vivacity of the child with the physical and mental activity disappears. They do not want to play with other children, become easily exhausted, complain of pains in the joints after every exertion and rapidly emaciate. A carefully selected dietary and good nursing may

possibly coax back the old vigor but it is never more than a coaxing.

In the meanwhile thirst, which had for a time been in abeyance, reappears and the quantity of urine increases two to four times the normal. The urine contains large amounts of acetone, diacetic and oxybutyric acids and ammonia and the breath has the odor of acetone exactly the same as in adults. The fully developed picture of diabetic autointoxication (diabetic acidosis) is now evident. The urine is rarely free from albumin although the quantity is small. Under the microscope the so-called coma casts are seen soon after the first appearance of the iron chloride reaction and their number markedly increases toward the end of life. I found the largest amounts of pathological acid, metabolic products among children under seven years of age in a boy of four years, 4.2 grams of acetone, 38.5 grams of oxybutyric acid and the urine contained 4.5 grams of ammonia in an excretion of 10.2 grams of urea. In this patient I determined the finding, repeated in other cases, that the uric acid was abnormally abundant on an absolutely purin free diet (eggs, vegetables, butter, cream, oatmeal): 0.6–0.87 grams per day while the nitrogen excretion balanced the intake. This indicated an enormous nuclear destruction as the nuclein is the progenitor of uric acid and the other purin bodies.

The **termination** of diabetes in childhood, when an intercurrent infectious disease does not complicate it, is without exception death by coma. Its approach is usually made manifest by gastric disorders such as loss of appetite, nausea, vomiting, pain in stomach, spontaneous or on pressure. Increasing nervous irritability alternating with rapid relaxation, sleeplessness, and great muscular weakness are further symptoms. They often continue for weeks although commonly the disease runs a rapid course. No mention need be made of the complicating organic diseases occurring with diabetes and so common in the adult type since they are only suggested. Some cases have been found associated with an unknown functional change in the pancreas and disorder of the intestinal secretion (calculus formation in the duct of Wirsung with resulting cyst and destruction of gland). Severe disorders in the digestion especially steatorrhœa and azotorrhœa follow.

The **prognosis** is almost without exception unfavorable if the diagnosis of a true diabetes is certain. As already stated transitory glycosurias occur especially among children and these completely recover. R. Schmitz and G. Klemperer have mentioned such cases and I have seen several. Such diabetic glycosurias dependent upon transitory disorders of the pancreas must entirely disappear within a few weeks, if the seriousness of the prognosis is to be disregarded. There are also patients through whose entire life from early childhood to advanced age, a definite intolerance exists to large quantities of carbohydrates which is not progressive in character. These are benign cases.

I know a family, the father of whom showed from his sixth year glycosuria as soon as the quantity of carbohydrates exceeded 200 grams. This idiosyncrasy has continued without change up to the present time. In the daughter, glycosuria has never been detected. One of two sons had even in his fourth year the same idiosyncrasy as his father and continues to manifest it although now over thirty years of age. Father and son, with this exception, are perfectly healthy. The process has possibly been influenced by the fact that in both since the day of discovery of this condition, there has been a rigid reduction in carbohydrates.

With few exceptions the statement is true that true diabetes in childhood knows no cure, no matter how mild it may appear in the beginning nor how gradual its development in the first months or even years.

Treatment.—Treatment has no effect in preventing this sad result but may influence the duration of the disease. This has usually been given in the writings of others as one to one and a half years. The average duration of my cases, which were detected after their development into a severe type, was not much higher; one and a half to two years. Patients who came under observation in the stage of mild glycosuria lived three to six years. Only those are considered in whom the disease developed before the seventh year of life.

In spite of the hopeless prognosis, it is our duty to prolong life as much as possible. The treatment will vary with the stage of the disease.

As soon as the tolerance for carbohydrates has been reduced to nothing, or has gone beyond that, strict dietary rules need no longer be considered. Their value no longer equals the distress which the complete prohibition of the carbohydrates or the limitation of the proteid diet gives to the child. Carbohydrates, with the exception of sugar, are permitted and it is a matter of indifference whether emphasis is placed upon milk or upon cereals. Experience however will teach that the carbohydrates of oatmeal are by far best assimilated in the diabetes of children. It has been possible for me several times to reproduce for a time a marked tolerance for carbohydrates by an oatmeal cure. Langstein also noted favorable results from its use in children. In the oatmeal cure children receive nothing except a gruel made of 150 grams (5 oz.) of oatmeal, 150–200 grams (5 to 6⅔ oz.) of butter, 60–70 grams (2–2½ oz.) of Roborat or 4–5 eggs as a daily allowance and in addition some wine. This diet is continued 1–2 weeks and then gradually replaced by other food. The result is often marvellous in increasing the tolerance, which unfortunately does not continue. Alkalies are the only drugs to be considered unless there are distinct indications for other medication; 10–15 grams (℥iiss–℥iv) of bicarbonate of soda are administered daily to neutralize the acid products of metabolism and to prevent

acid intoxication. When there is a marked tolerance for carbohydrates at least to the extent of about 40–50 grams (1½–2 oz.) with a diet otherwise strictly free from carbohydrates (meats, eggs, green vegetables, fats), this favorable condition with complete physical and mental vigor of the child may be prolonged for a considerable period. To accomplish this, an exact knowledge of the limits of tolerance is necessary. The quantity of the carbohydrates allowed must then be kept within these limits and this should be alternated from time to time for several days with a strict carbohydrate-free diet. It is unfortunately impossible to arrange distinct schemata for such a diet since the excessive capriciousness of the taste in childhood makes each patient an object of special study. Schematic regulations are from their nature worthless.

It is a difficult matter for the child and still more for the relatives who are responsible to continuously administer carbohydrates and proteids below the limit which produces glycosuria and at the same time to satisfy the demands of the infantile digestion and the taste of the child. But it must be done if the child is to be brought through. This attempt has so rarely been scrupulously made, that little can be said of the general results of such treatment. It would be of great importance in many cases to carry through the dietetic treatment of the child in a sanitarium. with the mother or another member of the family. It might then be feasible to restrain as long as possible the advances of the morbid processes and thereby to give opportunity to the organism to overcome the disease in case it is not of a hopelessly malignant nature.

It is naturally senseless to recommend for diabetic children the cure at Carlsbad, Neuenahr or Vichy. Of drugs, none can be recommended. Many home remedies are praised for diabetes in infants as well as for that disease in adults but such praise is almost criminal. Alkalies should not be administered before the condition of the urine (acetone, acetic acid and oxybutyric acid) indicates the proximity of an acid intoxication. It is not wise to begin earlier as children do not bear alkalies well for a long time and frequently digestive disturbances result from their use.

When diabetic coma occurs the attempt can be made to overcome it by intravenous infusions of a 3 per cent. solution of soda. It has been possible in some cases to get a good result, the fatal termination however is only postponed.

DIABETES INSIPIDUS

BY
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DIABETES INSIPIDUS is a disease characterized by the secretion of an abnormally large quantity of urine which contains no sugar and shows no affection of the kidneys. The concentration of the urine is relatively less than the quantity; the specific gravity often registers 1.005 and lower and the color is abnormally light. The great loss of water through the kidneys increases the thirst (polydipsia) and diminishes the excretion of water by the skin, which as a rule is dry and roughened.

The disease is rare—rarer than diabetes mellitus although relatively more frequent in childhood. Ten to fifteen per cent. of the total number affected occur in the first decade but the majority of these in the second half of this decade.

Etiology.—A constant pathologic-anatomical basis for diabetes insipidus has not been discovered. Diseases of the cerebellum and especially of the medulla may show evidence of diabetes insipidus but it is doubtful if these cases are identical in their pathogenesis with those in which no anatomical lesion of the brain whatever is found. Cerebral concussion also plays an undoubted rôle. Polyuria often develops towards the end of an acute infectious disease, increases to a distressing degree, continues many weeks beyond the primary disorder and then gradually returns to normal. This condition should not be classified as true diabetes insipidus but at most as a symptomatic form of the disease. The etiology and pathogenesis are generally unknown.

Symptomatology.—Diabetes insipidus, if it is not a postinfectious polyuria, is practically always a serious disease in childhood whether it develops in the train of a cerebral disease or appears spontaneously. Children suffer much from the distressing thirst, take no pleasure in their play or work, become irritable and quickly exhausted. A gradual emaciation almost always occurs, due to the difficulty of administering sufficient nourishment because of the large quantity of fluids which they drink. Considerable loss of heat results from raising this large quantity of fluid, usually drunk cold, to the temperature of the body. I estimated in one patient, a boy ten years of age, that this loss of heat increased the calorimetric needs of the body about 13 per cent. more than normal. These children usually are for their age markedly deficient in growth and especially in the development of muscle

and bone. No other change in metabolism has yet been discovered. Although the secretion of urine may reach three to four quarts in moderately severe cases, and seven to eight quarts and more in severe cases even in children, the constituents of the urine (urea, uric acid, mineral salts) are present in normal amount. The urine often but not always contains inosit, the significance of which however is still in doubt.

Other symptoms and retrograde changes are lessened perspiration, often some reduction in the temperature of the body, marked concentration of the blood serum, trophic changes in the nails, defective growth of hair, rarely forms of neuritis, especially optic neuritis.

The **diagnosis** is easily made from the symptoms. It is only necessary to decide whether it is a true diabetes insipidus or a symptomatic polyuria.

The **prognosis** and **course** cannot be predicted with certainty. It is dependent in diseases of the brain much more upon the primary condition than upon the diabetes insipidus. When the disease occurs spontaneously and becomes fully developed, it usually goes on to a fatal termination by gradual exhaustion or by some intercurrent disease (tuberculosis) for which it furnishes the soil. The prognosis however is not nearly as serious as in diabetes mellitus since complete recoveries and in other cases improvements have occurred. A well-defined polyuria and polydipsia may continue through life and be regarded as an inconvenience rather than a disease.

Treatment is not entirely without effect. Systematic, careful and graded restriction of fluids may produce beneficial and permanent results. I have seen several of these favorable cases among children. Hospital treatment is often more effective than that at home. Exclusive diets, as meat, milk or vegetable, have been strongly recommended but cannot be enforced. The care and nourishment should be directed to strengthening the body as much as possible. The question has recently arisen if it would not be possible to reduce the exchange of fluids in the body by a salt free diet and thus induce a gradual return to normal conditions. This deserves further investigation. Recently a child suffering with diabetes insipidus recovered under this treatment in my hospital service. Everything which stimulates the peripheral circulation is to be recommended. A constant out-of-door life has often a marked effect upon the polyuria and polydipsia. Favorable results have been reported from the use of the sulphur baths at Kreuznach and Nauheim and recently air and sun baths have been extolled.

Almost every drug has been tried and especially opium, belladonna, strychnine, ergotin, pilocarpin, antipyrin and the salicylates, recently adrenalin. On account of the great uncertainty in their action only the temporary use of such powerful drugs has seemed justified in children.

LYMPHATIC CONSTITUTION, NEURO-ARTHRITISM AND EXUDATIVE DIATHESIS

BY

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TRANSLATED BY

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MANY decades ago as well as quite recently, alterations in the conditions of the body, called constitutional anomalies, have been described under the above names. These find their expression in an abnormal "*habitus*," in a predisposition to certain organic diseases and in a number of functional disturbances. The descriptions of different authors do not make it clear, if the three names we have quoted above (to which we might add many others) are really synonyms for the same disturbance or if we have to assume different anomalies of this kind which have only some common symptoms.* This question has to remain open as long as we do not know more about the nature of these disturbances nor possess a reliable biochemical criterion for their recognition.

Some authorities do not like what appears to be the oldest term, that of "lymphatic constitution" (also "lymphatism" or "lymphatic diathesis") because, as they say, the swelling of the lymph-nodes is secondary and, at that, not always pronounced; they forget, however, that originally this name had nothing to do with the lymph-glands; it is an appellation handed down to us from the times of humoral pathology, according to which the trouble was founded upon an abnormal condition of the lymph, to which noxious humor many symptoms were referred; this is to-day not even called real "lymph" any longer, but no more should it be regarded as a true exudate according to our present views about the inflammations.

To-day one thing is certain, namely, that the practical importance of these disturbances is very great on account of their frequent occurrence; and any one who does not make the mistake of some specialists, in regarding each and every manifestation of these "diatheses" as a separate and autochthonous disease, will meet them daily and may even be in doubt if there is any other habitual symptom (except the malformations) that is not related to these conditions. In the author's

* French pediatrists usually regard "lymphatism" as one of the forms of "arthritism," thus subordinating the former term under the latter one. Escherich considers lymphatism (habitus 1, page 234) and what he calls exudative diathesis (habitus 3, page 234) as different affections.

Heubner does not see any valid reason why we should do away with the good old-fashioned names of lymphatism or lymphatic diathesis. The name of arthritism is not any better but we have to keep it up to understand the French literature.

opinion there is no valid reason why we should not go very far in this and include all stages of childhood. To this we are forced by our own personal investigations no matter what others have to say to the contrary.

Under these circumstances it will be easily understood that we can not attempt to give in this chapter a clear, precise and rounded-off description of these conditions; the so-called symptoms of these abnormal constitutions will mostly be described in other chapters of this work, still the editors of this work considered it necessary that we should give a short sketch of these conditions of which we used to hear a great deal years ago and which have lately been taken up again to a large extent, and this for the further good reason that we have made a good start in the rational treatment of these diatheses, the results of which can no longer be considered illusory.

The abnormalities of these children are in many cases observed in their *habitus* and their *disposition* and we differentiate principally between:

1. The *pastous, torpid* or *lymphatic-anæmic habitus.* Skin and mucous membranes are bloated, pale, fallow; the muscles are flabby and spongy; the skeleton, especially that of the face, is coarse. Hyperplasia of the lymphatic system is shown in the swelling of the visible and palpable glands, especially adenoids (adenoid face). The children are cross, lazy, frequently sleepy, absent-minded, stupid and of a phlegmatic (lymphatic) temperament.

2. The *erethic* or *neuro-arthritic habitus.* The skin is tender, the eyes bright, the pupils wide, the cheeks change their color frequently. These children are usually skinny, gracile, restless, lively, impulsive, irritable, also very bright, often precocious and highly intelligent; their disposition is changeable, they incline to affectation; they are impetuous, flighty, exalted, unsociable and insufferable youngsters, frequently with pronounced but one-sided talents (dégénérés supérieurs).

3. The *plethoric-obese habitus.* Amongst these we may group the so-called "prize-babies" of supernormal weight, tremendous adipose tissue, red cheeks, well-colored mucous membranes, who are inclined to free perspiration.

Occasionally obese children may take on the neuro-arthritic habitus after the second year, or the pastous habitus may be less clear later, etc.

Similar types have been differentiated among the scrofulous children, and this we can explain by the close relation between lymphatic constitution and scrofulosis. This had been recognized for a long time but has been explained satisfactorily only quite recently; of this we will speak again later.

Symptoms.*—In the older literature the picture of lymphatic diathesis is frequently inaccurate owing to the admixture of scrofular

* The following symptoms may appear in individuals with any one of the types of habitus just described but the frequency of the different manifestations varies considerably.

symptoms. The French descriptions of the constitutional abnormality in children, called "arthritism," especially those of Comby (1901, 1902), define this picture quite clearly. From the description of this last-named experienced and careful observer we can give here only an enumeration of the most frequent symptoms, or better, of the disturbances due to this diathesis.

General Symptoms.—Rises in the temperature without any apparent cause of the type of an intermittens quotidiana, lasting a few days at a time, together with chills, heat and perspiration, and which will return again and again after intervals of some months. These may change to true attacks of gout, thus forming their equivalent, or they may assume the character of a subcontinua* lasting for some weeks. The fever may be accompanied by headache, fainting spells and considerable weakness.

Systematic swelling of the lymphatic tissues, especially the *pharyngeal and faucial tonsils, of the glands around the throat, the jaw and the neck* (polyadenopathy and micropolyadenopathy); chlorotic condition of the blood; periodic anæmia.

Circulatory Apparatus.—Pseudohypertrophy of the heart with palpitation (so-called hypertrophy of growth), accidental cardiac and venous murmurs, habitual or intercurrent bradycardia and arrhythmic pulse, paroxysmal tachycardia; also various other vasomotor phenomena.

Respiratory Apparatus.—Relapsing catarrhal processes in the upper air-passages, coming on very suddenly (spasmodically) principally from colds; for instance *coryza* (with epistaxis), hay-fever, laryngitis, *diffuse tracheobronchitis and bronchiolitis, pseudocroup, bronchial asthma;* acute "pulmonary congestion," pleuritic irritation.

Digestive Tract.—This is a frequent seat of symptoms. *Anorexia;* parorexia (pica), *bulimia, fætor ex ore;* spasms of deglutition (œsophagism), coated tongue especially the so-called *lingua geographica* (Besnier as quoted by Marfan, Betz). *Recurrent pharyngitis, angina pharyngea and palatina,* dyspepsia with atonic symptoms and colic; habitual constipation and enteritis muco-membranacea either with or without the discharge of concretions (intestinal sand); appendicitis; cyclic vomiting with acetonæmia; hæmorrhoids.

Genito-urinary Tract.—The urine has frequently a high specific gravity and has a sediment of uric acid, urates, phosphates and oxalates. Intermittent albuminuria in some cases of the orthotic type; less often glycosuria; polyuria and pollakiuria; vesical tenesmus; enuresis nocturna; catarrhal cystitis and urethritis; vesical and renal sand or concretions accompanied by renal colic; movable kidney; *balanitis* (*non-gonorrhœic*), *vulvovaginitis;* dysmenorrhœa and metrorrhagia.

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* The author is inclined to include here the habitual rises in temperature (38° C. to 38.5° C. rectal) in some children (who give a negative Pirquet reaction).

Nervous System and Organs of Sense.—All kinds of *disturbances of sleep* especially nocturnal restlessness; pavor nocturnus; spasmus nutans; chorea (but not Sydenham's type) and choreiform restlessness; stuttering; convulsions, especially at the beginning of infectious diseases; laryngospasmus; migraine, neuralgiform pains, sciatica; *blepharitis*.

Motor Apparatus.—Rheumatoid affections; arthralgias, ostealgias, usually without any objective changes in the joints, but sometimes with periarticular œdema; rheumatic or spasmodic torticollis, lumbago; in exceptional cases true gouty affections with attacks quite similar to those in adults.

External Integument.—The skin is tender and over-sensitive to all kinds of external irritations, especially heat, great liability to freezing; evanescent œdemata, *hyperhydrosis, quick changes in color; urticaria; pruritus, prurigo, strophulus, intertrigo* and most frequent of all *chronic eczemas* either of the weeping, crustous and impetiginous type or in tough dry plaques together with seborrhœa; the former kind mostly in infants as the so-called *crusta lactea* of the face and scalp, the latter on the neck, back, chest, shoulders and arms, frequently symmetrical; true seborrhœa, especially *seborrhœa sicca* of the vertex; rarely only pityriasis, acne, keratoses, trichophytoses.

Four years later, in 1905, Czerny described under the name of "*exudative diathesis*" a disease which was in danger of disappearing from medical literature. He considered those symptoms as most characteristic which we have printed in *italics* in Comby's symptomatology so as to avoid repetition. But these do not, by any means, give an exhaustive picture and Czerny mentions many important details; though we must regard it as very strange that he should not have observed any symptoms referable to this diathesis in the digestive tract (with the exception of geographic tongue); whilst he includes the phlyctenæ which all other investigators (with the exception of A. Schütz and Moro) have eliminated and considered as part of scrofulosis. Czerny as well as Moro insist upon the importance of the circular caries of the incisors, and quite recently Czerny regards a premature flattening of the weight-curve during the first half year of life as a sign of exudative diathesis.

To-day we are still unable to decide, if we should regard the narrowing of the syndrome by Czerny as against the French school of pediatrists as a progress, though we will not deny this being likely. One explanation for this difference of opinion may be found in the fact that Czerny in his first reports considered almost exclusively the symptomatology in very young infants.

Etiology, Pathogenesis and Origin.—Older authors found the origin of these abnormalities mostly "in a distemper of the entire lymph-system" which was supposed to be accompanied by a faulty, *i.e.*, either a "sluggish" or an "acrid" condition of the lymph, leading to lymphatic

stasis and thus to congestion in and hardening of the glands (Jörg, 1826). It deserves special mention that even at that early date the following were mentioned as causes: 1, heredity; 2, over-feeding and an improper choice of food in infancy, in some cases even mother's milk was considered an improper food; 3, respiratory damages and other hygienic deficiencies.

It was no more possible at that time than it is to-day to give a clear-cut differentiation between the causes of the (latent) diathesis as such and the particular factors which evoke its external signs.

We can not give here the details of similar hypotheses nor of other older ones.

Bouchard (Maladies par ralentissement de la nutrition, Paris, 1882) places arthritism together with diabetes, gout, asthma, obesity, lithiasis, migraine, etc., into one group, namely the bradytrophies, *i.e.*, those disorders which are based upon an habitual slowing of metabolism. Space does not permit us to go into Bouchard's views, which have not been accepted in Germany, though Bergmann has quite recently proved the occurrence of an endogenous and truly constitutional type of obesity and has thus supported materially these theories. Comby's definition of arthritism in conformity with Bouchard is that of: "an habitual disturbance of nutrition transmitted by heredity" and he characterizes it as "the diathesis of wealthy and civilized nations, the dyscrasia of an urban population and of the intellectual classes, the vast degeneration of races which suffer from exhaustion due to the overloading of stomach and brain." He claims that an insufficient digestion of assimilable foods and also a disturbance of the internal metabolism lead to intoxication and thus to the symptoms.

We are inclined to think from what Bouchard has taught us, as well as from certain conditions of the urine and still more from our therapeutic successes, that the arthritis of children might be a true "uricémie" (an uric acid diathesis) and thus of the nature of an infantile equivalent of true gout; though we have not yet sufficient proof for this view, neither is the opposite proved, in spite of the careful investigations of Göppert. As far as we are aware none of the fairly conclusive biochemical methods of examination of the gouty disturbances of metabolism have been carried out in "arthritic" children (such as the quantitative changes in the elimination of the purin-bodies under a purin-free diet, the reaction to consequent addition of purins to the diet, the quantitative analysis of the blood for uric acid, etc.).

Comby places most importance on the factor of homologous and heterologous heredity for the occurrence of the arthritic diathesis, and he does this based upon the observation of a large number of cases. He finds in the parents and other nearest blood relatives of these sick children a remarkable frequency and gravity of the bradytrophic diseases of Bouchard (see above), as well as all kinds of neuropathies and psychop-

athies. Long-continued observation of single patients as well as of whole families help him, not only in recognizing the relation of the different symptoms depending upon this constitutional abnormality, but also to define their limits.

Heubner finds the cause of lymphatism in a congenital tendency towards an excessive hyperplastic reaction of the lymphatic tissues. He claims that a certain external injury, a specific agent, should not be sought for on account of the frequency of the condition, which, according to this author, is found in all degrees down to the more pronounced development of the infantile lymphatic apparatus which may be considered as physiological and might be regarded as "a function of development, of growth itself." Infectious and alimentary injuries may, however, act as a stimulus.

Czerny regards his exudative diathesis as a congenital abnormality observed in the descendants of pathologic parents, an inherited deficiency of the organism, and he finds this deficiency in the chemistry of the body, in an insufficient supply in the newborn of certain materials, of reserve-matter, which is gradually used up in extra-uterine life and which is therefore prematurely exhausted in unfavorably predisposed children. He considers this unfavorable predisposition not as a consequence of any kind of bodily inferiority of the parents (from alcohol, lues, tuberculosis, etc.) but as a specific family-disease.

This hypothesis of Czerny is amenable to experimental investigation (analysis of the composition of the tissues, of the physiologic-chemical condition of the organism, of metabolism). Similar questions have been discussed ten years ago in the investigation of exudative diathesis (which was then still called "scrofulosis"), though no positive results have come from this to date. Czerny regards as one strong argument against its connection with gout the reversed disposition as to age and also the reaction to a meat-diet.

Moro, who has made a thorough clinical analysis of lymphatic diathesis, finds its most important peculiarity in a special congenital disposition of the system for obstinate inflammatory reactions with exudation of "lymph," in which the lymphatic tissue plays an important primary as well as secondary rôle. He attempts to trace this predisposition to an "angioneurotic inflammation" (as it was called by Kreibich), to an abnormal function of the sympathetic nervous system and he puts special stress upon the neurogenous origin of the symptoms, especially from thermic, toxic and infectious stimulation.

According to the older as well as to the more recent investigations, the following conditions are of the greatest importance in causing the manifestations of the lymphatic (exudative) diathesis:

1. **The Kind of Diet.**—The diet may have a two-fold influence according to the latest publications of Czerny.

(*a*) Owing to the unfavorable development peculiar to exudative diathesis (the insufficiency in reserve material) human milk (as well as cow's milk) is an insufficient food as regards its plastic properties; exclusive breast feeding (as well as exclusive feeding with cow's milk) will, therefore, favor the appearance of the symptoms. About the therapeutic consequences, see below.

(*b*) Other digestive disturbances will also produce symptoms of exudative diathesis. Most ominous are the digestive disturbances expressed by the different types of obesity (principally retention of water in the body). In cases in which there is an unfavorable predisposition, these disturbances will cause, next to infectious injuries, most frequently the syndroma of a systematic swelling of the lymphatic organs. Rhazes, who lived a thousand years ago, knew of this, and more recently, amongst others, Flesch has mentioned it (in Gerhardt's Handbuch, 1878).

The author himself has raised the question, if it was not possible that under certain conditions (an unfavorable predisposition as to the functions of intestinal and cellular digestion) foodstuffs ingested into the gastro-intestinal tract might act in the body like an antigen; if this should be the case, then it would be quite natural to assume that the lymphatic diathesis represents a kind of food-allergia (food-anaphylaxis) and to explain thus the over-sensibility of the tissues against the group of originators of the allergic condition.

2. **The Condition of the Nervous System.**—Irritations of certain nerve-regions, especially of the sympathetic system, also psychic alterations have a tremendous influence upon the pathogenesis of this affection.

According to Czerny, the eczema of these children, for instance, is frequently the consequence instead of the cause of the itching and scratching; he claims that it is caused by the primary sensation of itching and that it can easily be cured by psychotherapy. The vasomotor disturbances do not only cause the quick changes in the color of the external skin, hyperidrosis, etc., but also hyperæmia and catarrhal swelling of the mucous membranes. Upon the mucous membrane of the pharyngeal tonsils these swellings may cause the formation of crypts, the stagnating contents of which will cause inflammations and infectious processes by their putrefaction.

Czerny believes, however, that the neuropathies and psychopathies which we observe in cases of exudative diathesis are to a large extent not caused by this disorder, but are brought on by injudicious treatment, and that only some of these are hereditary abnormalities.

3. **Intercurrent Infections.**—It has been known for some time that these (for instance, measles, tuberculosis) frequently bring out the symptoms of exudative diathesis, or aggravate them when they had

already been present. Czerny explains thus, for instance, the appearance of the symptoms after vaccination.

We know, from old as well as recent experiences, that difficult dentition may have the same result, and this brings before us the question if we should not in this also regard the sensitive irritation as the principal causative factor.

4. **Catching cold** is regarded by Moro and others as a most important etiological factor.

Relations of Lymphatic (and Exudative) Diathesis to Scrofulosis.—These two conditions have been mixed up with each other a great deal in olden times as well as recently. Some of the older investigators, however, knew the difference remarkably well from their exact clinical observation; they, therefore, attempted to differentiate a prescrofular stage (Jörg's "Skrofeln," Henke's "scrofular disposition") from the real disease ("Skrofelnkrankheit-scrofulosis" according to Jörg, "developed scrofulosis" according to Henke). It was only after we had realized that scrofulosis represents a form of tubercular infection and after we had learned more exact methods of proving this (Koch, Pirquet and others), that we were able to follow up successfully its relation to lymphatism. It was soon shown that the lymphatic constitution forms the soil upon which an accidental infection with tuberculosis will lead to the development of scrofulosis. The lymphatic diathesis is not so much (as we used to think) a special predisposing factor for the tubercular infection, as one which will rather influence the course of such an infection if it should arise accidentally. Escherich similarly expressed this contemporaneously and independently as follows: "Scrofulosis is that type of infantile tuberculosis which originates upon the soil of a lymphatic constitution."

This is by no means the same as when Czerny calls scrofulosis "a combination" of exudative diathesis and tuberculosis and when he states that dietetic treatment can remove the former and thus change scrofulosis into tuberculosis, and further that this is the only result of the institutional treatment of scrofulosis.

As the inflammatory reaction is the most effective defense of the system, we will understand that tuberculosis will find less favorable conditions upon the soil of a lymphatic diathesis as this is especially disposed towards inflammatory reaction; for this reason scrofulosis should be regarded as a relatively benign type of tubercular infection (Moro).

Relations of the Lymphatic Diathesis to the Status Thymico-lymphaticus.—This condition which has been described as well as named by Arnold Paltauf, the occurrence and importance of which in childhood has been recognized by Escherich, will be described elsewhere in this work (Vol. III). Here we will only mention briefly that Heubner, Escherich, Czerny, Feer and others regard the status thymico-lymphaticus

as closely related to the lymphatic diathesis and that they consider the former as a special type (perhaps to some extent an extreme type) or a part of the latter. Nothing definite is, however, known about this.

Occurrence.—The frequency of these constitutional abnormalities is very great; it is by far greater than that of manifest tuberculosis and it at least equals in infants that of rachitis, though it remains much longer in a florid stage than this latter disease. The manifestations frequently appear during the first three months of life, to persist beyond the puberty of the patient. In other cases puberty or even the end of the first decade will mark the turning-point. In adults we never observe the same symptoms which are so characteristic in childhood.

The urban population and of this again the upper classes are most severely and most frequently affected according to Comby; though it would appear as if statistics were so far of little use, owing to the indefinite meaning which the term has had up to now.

Anatomy.—In so far as organic changes have been found at post-mortem in the bodies of lymphatic children—in wasting diseases all its signs disappear—they are very similar to those found in the status thymico-lymphaticus (confer *ibid.*).

Quite recently Bartel has attempted to describe the histological picture of the lymph-nodes in the latter disorder. He states that we have to deal with the consequences of a faulty development which is found originally not so much in the lymphocyte tissue as in the connective tissue; only later will the secondary atrophy of the follicular apparatus be noticeable. The frequent concomitant hypoplasia of the blood vessels might play a leading rôle genetically in the under-development of the connective tissue of the lymph-glands which dates back to embryonal life and also of other coördinated symptoms (such as insufficient development of the genital organs, malformations of all kinds: "the hypoplastic constitution").

Treatment.—In conformity with the very ancient recognition of the fact, that faulty feeding, especially over-feeding, and other faults in the method of living produce the symptoms of this disorder, we can observe that through the therapeutics of the different decades and the different nations runs like a red thread in a fabric the treatment with diet, fresh air, baths and change of climate.

Comby, who regards this affection as a degeneration due to civilization, recommends the "retour à la nature" all along the line, long-continued breast-feeding for infants, principally vegetarian diet for older children (not more than 3 meals daily, consisting of bread, soups, eggs, milk, vegetables, pastry, fish and white meats, stewed fruit,—but without spices, acids or too much sugar), further hygiene of the skin with hydrotherapeutic measures, gymnastics, sun-baths, etc. The spas recommended are La Bourboule, Chatel-Guyon, Contrexeville, Mont-Dore,

Vichy and others, the drugs employed are alkalies, the alkaline salts of organic acids, nux vomica, digestive ferments, etc.

Czerny recommends the following diet in exudative diathesis: During the first two years of life we give the smallest amount of milk on which the infant can thrive; in breast-babies we must therefore reduce the number of meals and the length of each meal; should considerable fat be deposited in spite of this limited supply of milk, then we will have to replace part of the milk by carbohydrates, soup and vegetables as early as the second quarter and at $1\frac{1}{4}$ or $1\frac{1}{2}$ years we give the diet for older children, which latter should be principally vegetarian, though we add small amounts of milk ($\frac{1}{2}$ to 1 pint daily) and of meat. Eggs are not permitted, nor cream, butter or sugar. This will sound familiar to those who remember the directions Lahmann used to give.

Following is the sample of a menu for a child in the second year of life according to Czerny: First breakfast, milk diluted with coffee or tea with bread or rolls without butter; second breakfast, fresh fruit; dinner, thick soup (especially the purée of the legumes), minced meat, fresh vegetable (spinach, carrots, cauliflower, salad, string beans); afternoon, milk diluted with coffee or tea, rolls; supper, minced meat with bread (or potatoes or rice) and (very little) butter; as drink, weak tea or water.

Czerny also considers psychic treatment of the greatest importance. He claims that not only the nervous symptoms proper but also asthma and skin-affections (obstinate eczemas covering almost the whole body) can be cured rapidly by improving the child's mind; that it is necessary first of all to distract the child's attention from its somatic condition, and that rest cures are bad and fattening or similar cures still worse; that medicinal treatment, also, is of no use. One must not show any special anxiety nor bring up the child with the idea that it is ill. Frequently a radical change in the child's mode of living and education is needed: removal from its home and attendance by strangers; it is also of great importance that it should be thrown together with children of its own age and not with its brothers and sisters only.

Prophylaxis is almost identical with the treatment itself as it is only possible to recognize the condition from its manifestations. By avoiding dust and smoke in the air and also the exposure to contagion we are able to prevent the causative infectious diseases. A favorable climate (but not a spa according to Czerny) for a prolonged sojourn in summer is advisable.

Infectious Diseases

MEASLES

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Measles is one of the commonest infectious diseases of childhood. Jurgenson gives the eighteenth century as the date of its definite recognition as an epidemic disease. The first important clinical and epidemiological article, dealing particularly with the incubation stage, was by Panum in 1846 giving his observations during an outbreak of measles in the Faroë Islands. Since that time much has been done and published from many sources confirming Panum's observations. In the year 1875 the interesting opportunity again occurred to observe the development and spread of this infectious disease, in an outbreak so severe that the inhabitants were cut off from communication with the outside world.

Etiology and Pathology.—Measles is produced by an unknown virus which is of a relatively evanescent nature. It is not possible to carry the disease any great distance by a third person or by means of living objects. The virus is short-lived outside the human body and presumably can propagate only within the human body. Whether or not the virus of measles can remain latent in one who has had the disease is still a question.

Time and Mode of Transmission.—The transmission of the disease from infected persons occurs most easily during the so-called initial or prodromal stage, and at the time of the rash. In the last or stage of convalescence the danger of transmission is not so great. These two first mentioned periods of measles are particularly well adapted to the dissemination of the disease in that during the catarrhal involvement, which predominates and in the course of the sneezing, snuffling, hawking, and coughing, the infecting organisms multiply in a most energetic manner, and a still more infective virus is produced. The greatly increased secretion assists in transmission. I recall a case, however, admitted to the Hospital for a subsequent diphtheria, on the fourteenth day after the appearance of the rash, which infected children in the same ward. On the fourteenth day after the admission of this child to

the hospital the eruption of measles appeared simultaneously in many of the patients. This case demonstrates perhaps, the oft-times striking stability of the virus of measles in persons recently infected. Measles very readily attacks those who have not previously had the disease. In consequence it always occurs in great epidemics in thickly peopled areas, returning year after year, particularly in those seasons in which catarrhal conditions are most apt to occur. Conditions which bring together a great number of young persons are favorable to the spread of measles, as for example the schools, playgrounds, children's entertainments, etc. The transmission of measles can result, (1) through direct contact with an infected individual; (2) still much more often the conveying medium is air infected with the poison, and (3) the possibility of infection through the secretions of the mouth, the nose and the respiratory tract, also the blood, lymph, and tears, conveyed by persons, animals, or infected objects.

Indirectly the desquamation from the skin may by reason of its infective nature contribute in the transmission of the disease.

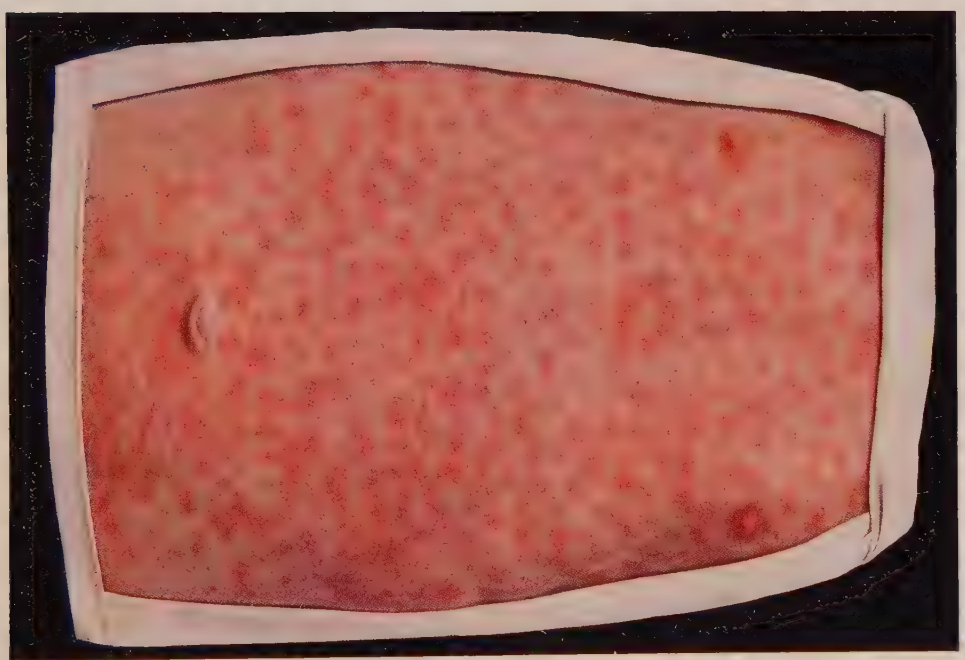
The most important carrier of infection in an indirect way is infected air which, with the help of particles of dust or water drops, serves as a means for spreading the infection, although only for a short distance, as the virus is short-lived in the air. As a result it happens that epidemics of measles occur in the larger cities and more thickly populated districts to a greater extent than in the more sparsely populated parts.

There are, it is said, few persons who are immune to measles, for the *predisposition* of man to the disease is particularly great. Measles is mostly acquired in childhood, the period of life which shows an especially high grade of susceptibility. Adults experience, as in many diseases, more discomfort than younger persons; nevertheless it attacks them much more lightly. The predisposition to the disease in later life is only apparently less, and I have seen a woman sixty-eight years old with measles. The idea that a lesser susceptibility to measles exists in the first six months of life as compared with the later period of childhood, is certainly not correct. Children under six months of age show a diminished intensity of the symptoms, sometimes they are only of a rudimentary character, so that the disease may be overlooked, or a mistake in diagnosis be made. They contract the disease on exposure just as readily as other children.

The occurrence of two attacks of measles in the same person is rare. In most instances there was a mistaken diagnosis, especially if the first infection should run a milder course than the second, but the occurrence of a second infection is not by any means to be denied. German measles, scarlet fever, infective erythema and other toxic erythemata (those following the use of serum and such as are of

PLATE 17.

a, Eruption of measles on the face.



b, Eruption of measles on the body.

intestinal origin) can likewise give rise to error in diagnosis. The outbreak in an acute form, of a fresh rash with associated catarrhal symptoms occurs before the measles eruption. It occurs less frequently in the above-mentioned conditions.

Symptoms.—From the day of infection to the outbreak of the rash is thirteen to fourteen days. The first signs of trouble are seen usually on the tenth or eleventh day of incubation. I observed on the sixth day before the outbreak of the rash, in a case of measles complicated with scarlet fever, a slight rise of temperature and abundant Koplik's spots on the mucosa of the mouth. A long initial or *prodromal* period of measles is sometimes found in sick and weakly children. This period, during which the disease reaches its full development, that is, from the onset of the symptoms to the outbreak of the rash, usually requires three or four days, and is marked by the following symptoms. At first there appear signs of catarrh of the upper respiratory tract and eyes and the child begins to sneeze. This sneezing may soon pass off, but often continues throughout the whole initial period. Epistaxis may occur with the hyperæmia of the nasal mucosa, or the irritation may come on quietly, and find expression in a severe coryza. The nasal secretion is at first serous or mucous, and it can also assume a purulent character. Severe catarrhal changes in the mucous membrane of the eyes are associated with the coryza and are shown by lachrymation, photophobia, and injection of the conjunctiva; the eyelids also show marked swelling, and adhere together in the morning on account of a mucopurulent discharge. The separation of the lids is painful as the dried discharges adhere to the edges of the lids and produce irritation. The signs disappear usually with those in the nose. An important part of the catarrhal symptoms are found in the throat and bronchi.

Fig. 42.

Measles without conjunctivitis.

The first definite sign of the approaching rash is a hyperæmia of the mucous membrane of the mouth. This is characterized by the presence of *Koplik's spots*. The credit is due to Koplik, an American

physician, of having drawn attention to this symptom which had been referred to in literature, but little studied until now. Three or four days, in rare cases somewhat longer, before the appearance of the rash there appears on the mucous membrane of the cheeks small bluish white, or yellowish white points, the size of a small pin head. They are usually surrounded by a small zone of reddened mucosa, which has the appearance of a general reddening with the fine white points upon it. This hyperæmia of the mucous membrane may be wanting. The white points are mostly on the level with the mucous membrane, and are less noticeable beside the strongly shining mucosa. They may be mistaken for milk particles or fungi. The white spots which are composed of epithelium, detritus and bacteria of the mouth adhere rather firmly to the mucosa and on removal expose an excoriated, even gangrenous appearance, instead of a smooth glistening mucous membrane. These are especially numerous on the mucous membrane of the cheeks and on the reflection on the gums, and less frequently on the inner surface of the lips. Punctiform hæmorrhages sometimes occur as the Koplik hyperæmia becomes less, and ulceration of the mucosa of the cheek is found as a result of maceration. The Koplik efflorescence usually begins to fade when the rash has reached its full development. These form a very frequent group of signs associated with the onset of measles, yet they are often wanting in the milder cases, especially in those occurring in the first year of life.

Fig. 43.

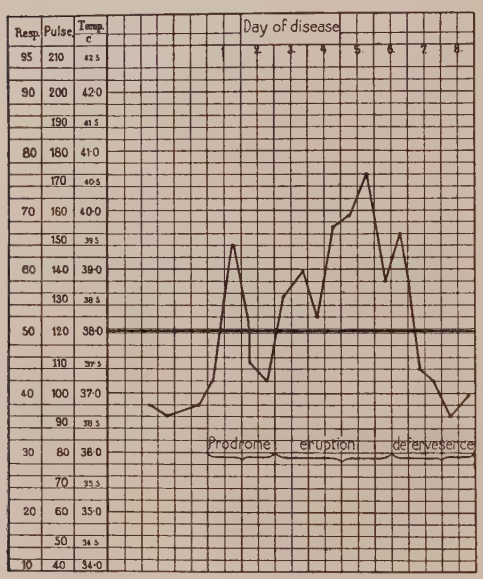


Chart I. Typical temperature curve in measles.

As a rule there is a characteristic measles rash on the mucous membrane of the mouth. It comes on suddenly, lasts but a short time, and shows itself usually somewhat later than the Koplik spots, situated principally upon the soft and hard palate, with greater intensity also on other parts of the cavity of the mouth. It occurs in the form of pale or light red irregularly outlined streaks or spots between which the mucous follicles rise. These are swollen to the size of a cherry stone, and can be seen with greater distinctness on account of the pale color of the mucous membrane of the palate.

Concurrently with the coryza, *irritation of the larynx* and bronchial mucous membrane become evident, the early cough is short and dry, and the severe paroxysms are annoying. With involvement of the larynx the cough assumes a barking character, and with still greater swelling of the subglottic laryngeal mucous membrane takes on the character of a pseudocroup, which with the diagnostic barking cough denotes a greater or less amount of laryngeal stenosis. This may be sufficiently great to produce slight attacks of dyspnœa. These laryngeal changes of the prodromal stage are however without danger to life, in contrast to those of pseudocroup, and croupy changes which sometimes occur in the period of convalescence and which may prove a serious complication.

Fig. 44.

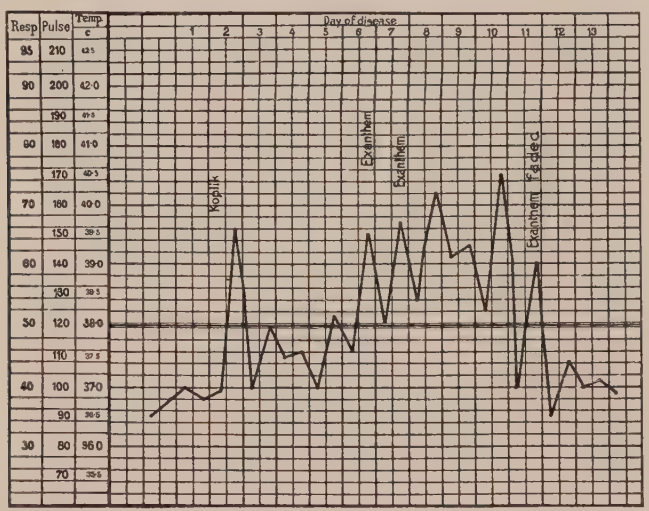


Chart II. Long prodromal stage.

Now and then in small children, or those weakly or tuberculous, the *bronchitis* of the early stage with its short dry cough extends to the smallest bronchi and gives rise to foci of bronchopneumonia, which in its further course is of bad prognosis. Usually the bronchitis is characterized on auscultation mostly by dry râles, and where there is expectoration it is invariably scanty and mucoid. With the outbreak of the rash there is a great increase of the cough, the frequency and dryness of which is distressing alike to the patient and those about him. The frequency of respiration which is the result of lessened blood aeration and of the high temperature, is increased to a distressing dyspnœa. This is made still more harassing by the increased bronchial secretion, and numerous and various forms of râles. With the fading of the rash all these respiratory signs subside, either at the same time or shortly afterwards.

The *temperature* in measles shows a fairly characteristic curve as the accompanying Chart I, (Fig. 43), will show. Frequently in the early stage the elevation of the temperature may exceed 39° C. (102° F.). It is usually not of long duration and gives way to normal or subnormal temperature for one or several days. With the first appearance of the rash the fever rises rapidly often to 40° C. (104° F.) or over, and usually assumes a continuous or remittent type until the fifth or sixth day of the disease when it falls by crisis. It goes without saying that this temperature curve is subject to many variations depending as it does upon the severity of the infection, the individual predisposition to temperature changes, and the occurrence of complications. It may be therefore, that this two pinnacle type of curve in measles may, according to the height of fever in one stage, take on another form of curve; usually however this particular type will be recognizable in it to a greater or less degree. A glance over the accompanying temperature charts should make the individual variations of the temperature course clear. Charts II and III show the association of Koplik spots and high temperature. There can be a still earlier appearance of the fever in relation to the Koplik efflorescence, so that the other prodromal signs appear first, and then the meaning of the rise of temperature is difficult for the physician to interpret; in any case a careful inspection of the mouth should always be made. With a more protracted initial stage the interval between the two rises of temperature will naturally be increased, sometimes the rise of temperature occurs first with the outbreak of the rash. Elevations of temperature after the normal defervescence and after the subsidence of the rash are mostly associated with complications (otitis, stomatitis, pneumonia, tuberculosis, etc.). A late fever of short duration, such as is shown in Chart IV for instance, may show no pathological reason for it. In slight cases, as also in nursing infants, I have often seen a striking afebrile course in undoubted measles.

FIG. 45.

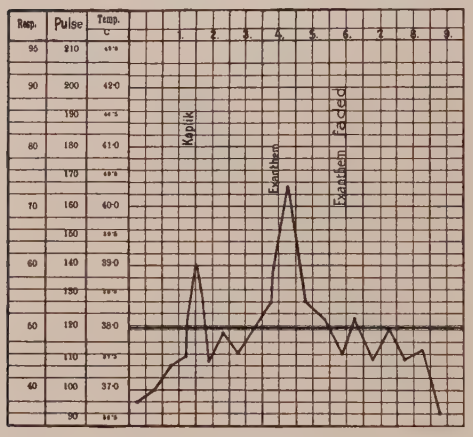


Chart III. High temperature on one day in a four and a half year old boy.

When the early stage has run its course with the symptoms described, the eruption follows as the diagnostic appearance of measles. Simultaneously in severe cases the catarrhal manifestations and the fever make their appearance in the most intense form. The patient

shows great lassitude, is dull and delirious, and in small children there may be convulsions. The general condition, and the other symptoms usually bear the closest relationship to the severity of the rash, the intensity of which is an index of the severity of the entire course. Very rarely there appears a slight transient erythema on the face, and particularly on the neck, two or three days before the general outbreak of the rash, but only three instances of this rash have come under my observation. The rash spreads according to definite rule over the skin, from the thirteenth to the fourteenth day from the beginning of the incubation. Exceptions from the typical spread or extension of the rash are found only in the milder cases.

The rash first attacks the head and region of the face, where the earliest appearance is at the margin of the hairy scalp, and the region behind the ears, and from there it spreads rapidly over the face particularly the temples and the region of the chin. It extends over the neck and downwards over the upper arm and trunk, its further course is over the forearms, hands, the thighs, and finally the legs and feet. It fades in the same order as it comes. The rash usually requires for its development and disappearance from three to five days according to its intensity, and leaves behind it a pigmentation of the skin which is visible for fourteen days or more. The rash at its height can cover the greater part of the skin surface at one time, particularly on the second and third days of eruption, both the fading and freshly appearing rash being from pale to bright red in color, occasionally of a livid tint. This latter coloring occurs in the more severe infections, with the onset of pneumonia, failing heart with lack of compensation, and other complications damaging to the heart and lung functions, such as myocarditis, croup, etc.

FIG. 46.

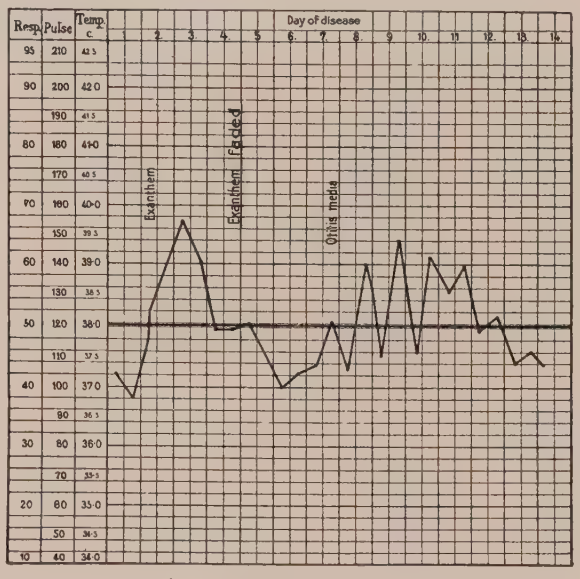


Chart IV. Rise of temperature during convalescence as a result of otitis media.

The *rash* often has a pale appearance in nursing infants, and in weakly, debilitated or crippled children. Usually the eruption varies in

size and form, from the size of a pin head to that of a cent, mostly irregular, and never exactly circular as one often observes in German measles. The rash does not begin on the surface of the skin, and in its further development is usually of a maculopapular character, which may easily be felt by passing the finger over it. The edges are not abrupt but fall away gradually. In young children we sometimes find, as a result of greater infiltration, that the individual spots are raised, map-like in form and with abrupt edges which can easily be confused with other forms of urticarial eruption. The single spots may run together into larger spots or patches, always leaving however greater or smaller areas of healthy skin between them, so that a mottled, even checkered

FIG. 47.

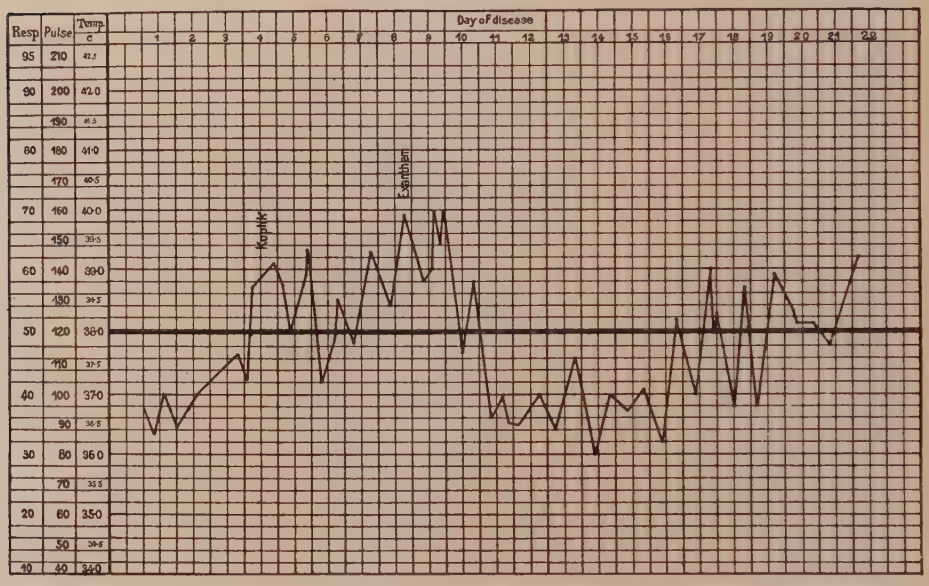


Chart V. Measles complicated with latent tuberculosis of the bronchial glands. Boy four years old.

appearance of the skin always occurs, and the designation in the lay mind of "spots" or "spotted sickness" is appropriate. When the finger is pressed upon an old erythema the skin remains a yellow or brownish color, especially in those forms of measles in which the rash shows blood infiltration and takes on a livid character. Effusion of blood into the skin is not uncommon and is absolutely no criterion as to the severity of the case. This can be produced artificially by raising a fold of the skin diagonally to its usual course and pinching it. This increased permeability of the vessels of the skin also exists in parts free from the rash. Hæmorrhages occurring at the outset of measles in sickly, or tuberculous children, are of bad omen. They occur in points or patches and often involve the whole of the abdominal surface. Some instances are recorded in the literature of *measles without an eruption* and the existence

PLATE 18.

a *b*

a. Eruption of measles on leg and foot.
b. Erythema infectiosum.

of such cases cannot be doubted, even if we question the diagnosis and the want of knowledge of the observer. Heubner was able to obtain the best possible opportunity to follow up this matter in observations upon brothers and sisters. Undoubtedly the best field for clearing up such caprices of the rash is that of private practice.

In close relation to the rash stands the *desquamation of the skin*, which in measles is an evanescent and slight matter and often entirely wanting. Exceptionally, however, it may appear in a very marked form and similar to that of scarlet fever. It differs from this in the fact that the hands and feet remain free, while on the face, neck, trunk, arms, and legs it is most evident. The face is chiefly involved and shows a marked peeling. The desquamation is usually fine and bran-like in character, but in severer cases it may occur in small flakes.

As a result of the measles poison, and the skin changes induced thereby, there is frequently a swelling of the lymph-nodes, chiefly those of the cervical region. Sometimes this swelling while only slight, attacks the whole lymphatic apparatus. The liver and spleen are not affected and show no appreciable enlargement. Fairly regularly there is a diminution of the leucocytes, but in the incubation stage a leucocytosis is observed.

The general condition produced by the grade of infection and combination of individual symptoms is dependant not only upon the severity of the illness but also upon individual peculiarity. The marked cerebral disturbances (convulsions, drowsiness, delirium) which appear in many febrile diseases in infants, fortunately are rarely seen in measles. Even the initial stage shows certain disturbances of the general condition, such as lassitude, prostration, apathy, headache, a sense of pressure in the eyes, subjective sensation of light, irritation in the throat, a sense of stoppage in the ears, symptoms all connected with the infection and the early catarrhal condition. With the progress of the disease the drowsiness is augmented and marked jactitation may appear. Pains in the joints, and lumbar pain is common particularly in adults. Loss of appetite, and at the same time rapidly increasing thirst are the common accompaniments of the period of eruption. The general condition usually improves rapidly as the exanthem fades, only the lassitude and swelling of the face are seen in this stage, just as peevishness is the common accompaniment of the stage of convalescence.

The course of measles in normal cases is well defined and as mentioned above may be divided into several stages. The whole period may be put down as about three and a half weeks. We differentiate thus: first, the period of incubation from the beginning of infection lasting ten or eleven days, and this leads to, second, the actual onset of the disease as shown by the outbreak of the catarrhal symptoms. This is the initial or prodromal period and lasts two to four days, so that on

the thirteenth or fourteenth day of infection we have the period of eruption characterized by the outbreak of the rash. The rash persists three to five days and within this period it fades and disappears. This period represents the crisis of the disease, and the passing into the stage of convalescence, which in uncomplicated cases rapidly and immediately closes the attack. For a week longer, on prophylactic grounds, isolation precautions should be observed.

Abnormal Course, and Complications.—These are ushered in by a fresh rise of temperature of a remittent or intermittent type, or no fall may occur, a lower grade be struck, and a continuous type of fever be maintained. The most desperate form is that described as septic measles, which within a few days runs a rapid course to a fatal issue. It is probably the lessened resistance of the individual to the virus of measles, that accounts for the severe signs of prostration, the high fever and the acute course of the disease, which toward the end of its course shows a striking similarity to the toxic forms of scarlet fever. It may occur at any time of life. While the blood findings in these fulminating cases of scarlet fever are always negative, in the blood of septic measles on the other hand a double infection with streptococcus is found. The parenchymatous organs always show marked degenerative changes.

During measles and following it, there are certain visceral complications which must be considered. The *skin* may first be mentioned. An obstinate *eczema* showing a variety of characters may be associated with measles; as for instance, fine nodules may develop and these may coalesce and awake suspicion as to the existence of a new form of measles rash. The rash is often pustular, pemphigoid, or impetiginous in character where there has been neglect in the care and nursing. Ecthyma with its indurated inflammatory base is also found in such neglected children, situated particularly on the buttocks, and in the genital regions. The tendency to necrosis of the skin and mucous membranes is marked but fortunately *noma* rarely develops. I once saw in the course of measles a well-marked dry gangrene of the prepuce, yet it was without hindrance to the ultimate recovery of the child.

A skin eruption only recently much observed is nodular in character and tuberculous in origin. The nodules are scattered, reaching that of a lentil in size, brownish in color, sometimes with a blue discoloration, often yellow, they are somewhat shiny in appearance, and the infiltration is sharply outlined; these are described as *tuberculides* (see article by Leiner in Volume IV. of this work). They are a definite expression of tuberculous infection, and are frequently seen in tuberculous individuals in association with measles.

The *respiratory tract* is the most frequent seat of complications. The measles virus alone or a mixed infection may work serious damage. The nasal mucosa undergoes inflammatory changes, and the resulting

swelling, particularly of the mucosa, may persist and interfere with nasal breathing. In children in the first year of life, as a result of insufficient care, the nasal secretions excoriate the skin about the nostrils, and the lips, as well as the nose itself, swell up and become the seat of scrofulous infiltration. The skin and mucous membrane thus stretched crack, and deep fissures may form which give the patient great pain, and in addition offer a favorable site for the entrance of various infecting organisms. Commonly micrococci are the cause of these septic fissures, not infrequently it is the bacillus of diphtheria. This latter organism readily infects the patient in the course of measles, and it is quite evident that as a result of measles, a distinctly lessened resistance to diphtheria is shown, and the nose, throat, skin, eyes, genitals, but the larynx in particular, are the points of implantation of this unusually rapid infection. The portions of the skin infected by diphtheria sometimes show an early and striking tendency to necrotic change which may lead to extensive ulceration.

Croup arising during measles is not always necessarily of a diphtheritic nature, yet this form often occurs. Sometimes a membrane forms in the throat, and may extend to the bronchi, yet repeated bacteriological examinations may fail to demonstrate the presence of diphtheria. This condition is recognized clinically by the more yellow color and loose adhesion of the membrane and shows micrococci alone or sometimes influenza bacilli. A peculiarity that may be mentioned is that in spite of the extension of the membrane into the larynx and below it, the throat may often be free, or show but little membrane. The signs of croup can be produced by swelling of the mucosa without the presence of any membrane whatsoever. Another cause of pseudocroup is an aphthous inflammation of the mucosa of the mouth and larynx, moreover without the laryngeal mucous membrane being affected. These so-called laryngeal signs may be produced by a marked inflammation as a result of an aphthous stomatitis spreading from the throat. The development of aphthæ in measles and scarlet fever is especially variable in character and extent. By reason of the tendency to necrosis it may produce extensive grayish yellow discoloration of the mucosa, *i.e.*, epithelial necrosis. Deeper losses of substance such as are so frequent in scarlet fever, are rarely found in measles.

Apart from the tracheobronchitis which commonly occurs and may be of a more or less severe type, *involvement of the lungs* is the most serious complication. Capillary bronchitis or bronchopneumonia occur comparatively frequently in the first year of life. Objectively they are evidenced by a sharp rise in temperature to 40° C. (104° F.) or higher, passing into a continuous form of fever, also by rapid breathing, dyspnœa and increasing unrest. Physical examination of the chest confirms this. Frequently the disease is bilateral, and the area of pneumonia is diffi-

cult to localize, especially when it is centrally situated; small foci, especially early in the disease, can readily be overlooked, particularly when there exists at the same time a generalized bronchitis of the smaller tubes, the latter not uncommonly causing atelectasis in young children by reason of the lessened entrance of air into the lungs. Capillary bronchitis and a spreading croupous pneumonia in the course of measles are most unfavorable complications.

In cases that recover, after the disappearance of the fever and the other acute manifestations, it generally requires several weeks before the normal note is found over the situation of the consolidation, the auscultatory signs of consolidation disappear somewhat earlier. On account of their slow disappearance Escherich terms these "asthenic pneumonia." They frequently raise a question as to the existence of tuberculous infiltration, from which however they are differentiated mainly by their further course.

In persons with latent tuberculosis, particularly of the bronchial lymph-nodes, a more or less widespread tuberculosis of the lungs may develop with measles. This may take the form of a local infiltration or a miliary tuberculosis with a marked rise of temperature.

There is still to be mentioned the acute necrotic pneumonia described by Heubner. In this the measles virus brings about an acute necrosis of the lung tissue and in the course of a few weeks the production of extensive bronchiectases. The rash is usually of a fleeting nature, fading rapidly and coming on long after the prodromal signs, and only shortly before death.

The peculiar course of the measles rash as well as the acute pulmonary complications may here be described in detail.

Among the laity these rudimentary forms are spoken of as "measles striking inward." After the appearance of such a rash, lung complications can safely be surmised. The rash shows a pale or bluish discoloration passing into a deep cyanotic appearance (with hæmorrhagic measles the coloration is brownish and livid). The mucous membrane of the lips, mouth and conjunctivæ are blue. The anxious expression, the movements of the alæ nasi and other signs of dyspnœa, the great restlessness, and collapse, complete the picture. It is mostly in children in the first year of life that these most severe and fatal forms are observed.

Frequently the lung affection in measles is brought about by a mixed infection with influenza. In the majority of systematic investigations carried out upon such forms of pneumonia, the influenza bacillus was found in the bronchial secretions. Whooping-cough which readily appears in association with measles, likewise gives rise to acute and chronic lung affections, especially in tuberculous subjects. They may also favor the outbreak of pleurisy, which is mostly of the fibrinous variety, but may also be serous or purulent.

The *heart* is seldom affected in measles. Frequently during the most severe period of fever a faint murmur may be heard for a day or two, without further injury being discoverable. The endocardium, myocardium, and pericardium each may suffer. As a result of measles rapid and failing heart action may arise, and myocardial changes are the features that remain, and by their severity impair greatly the general condition.

A transient *albuminuria* may occur during the febrile period without further injury to the kidney. Sometimes there is a nephritis analogous to that seen in scarlet fever. As to causation these cases of nephritis appear to be of infective origin, and not infrequently the assertion has been made that they are produced by the virus of measles, thus far however they have not been submitted to systematic pathological investigation.

In measles the frequent diazo reaction in the urine is an evidence, as in typhoid fever and tuberculosis, of an increased destruction of the albuminous bodies, and of a disturbance of tissue change.

The *eyes*, which suffer an acute conjunctivitis in the early stages show in the later course of the disease a tendency to chronic conjunctivitis and blepharitis. This is especially so in children of a scrofulous tendency or as the result of neglect. The conjunctivitis can proceed to the development of phlyctenules and finally to ulceration with marked photophobia and lachrymation and as a result, an extensive eczema of the face may be produced. The swelling of the conjunctiva and lids may continue with intense purulent discharge, in the further course of which I have observed one case of bilateral panophthalmitis which apparently had its origin in infective embolism, or in infection from without, the bacteria gaining entrance through an already poorly nourished cornea.

The *ears* are frequently the seat of catarrhal or purulent otitis media. This readily occurs in children suffering from adenoid vegetations, so soon as the rhinitis becomes severe, and the infection of the nose and nasopharynx extends into the Eustachian tube. The advent of otitis media is announced by a fresh rise of temperature, often of a high grade, and usually of an intermittent type. The child becomes restless, complains of the ears or of headache and puts its hands to its head. In younger children opisthotonos is frequent and mental dulness and convulsions commonly occur. These alarming symptoms disappear with the escape of the exudate through the drum-head into the outer ear. With protracted retention of the exudate, or if the suppuration becomes chronic, carious changes can occur in the bony structures of the ear, in the mastoid antrum or of the entire mastoid process. The objective signs of this extension are redness, swelling and œdema of the skin over the mastoid process, pain on pressure, and protrusion of the

outer ear. If the otitis media be one-sided and there occur a swelling of the lymph-nodes of the same side (which often occurs with otitis) then the diagnosis is clear.

Moderate swelling of the *lymph-nodes* is often present during and after measles. This swelling may be general while the rash is present, but more frequently it is confined to the cervical groups. In tuberculous and scrofulous individuals, particularly as a result of eczema, excoriations, etc., marked swelling of the lymph-nodes may occur in these groups, and even proceed to suppuration. The tendency to the proliferation of adenoid tissue is likewise evident in the region of the pharynx and a persistent enlargement of the tonsils may be noted. More frequently we find an enlargement of the adenoid tissue of the nasopharynx, which plays an essential part in the development of the nasal and ear affections so prone to arise after measles.

Although the lymphatic apparatus of the *intestine*, mainly the mesenteric nodes and Peyer's patches appear moderately enlarged, especially during the period of the rash, the part played by the intestinal tract is generally insignificant. Nausea, vomiting, and diarrhœa sometimes occur in the initial and exanthematous stages. The diarrhœa may continue until the disappearance of the rash if care be not taken. In young children the condition is more serious when the lower bowel is attacked, either alone, or in association with a former enteritis, and arises usually as the rash is fading or later. This lowers the resistance of the patient and forms a favorable basis for the development of other infections, especially pneumonia. The sharp outbreak of such an intestinal condition not infrequently leads to a fatal issue, by the marked exhaustion, intoxication and infection. The symptoms are at first those of a moderate intestinal catarrh, but soon the evacuations assume a mucopurulent character, which in turn give place to movements of pure pus with an admixture of blood; still later a frothy fermentation occurs, the stools have a curdled appearance, and a foul, sometimes putrid odor. The patient wastes rapidly, the color of the skin fades to a grayish tint, the eyes sink deep into their sockets, there is marked prostration, and finally collapse. With this there is a progressively lower temperature, sometimes the abdomen is much distended, very tender on pressure along the line of the descending colon, and particularly so over the sigmoid flexure.

The anatomical findings agree exactly with the clinical picture of a severe dysentery, in that the large intestine shows deep gangrenous, broken-down ulcers, often of great extent. The observations of Jehle as well as the gradually increasing study of these intestinal lesions point to the fact that we have to do with a secondary infection following upon measles, the latter favoring the sharp necrosis of the tissues.

The *nervous system* during the course of measles shows no particular disturbance apart from the general condition already depicted.

Exceptionally there may be mental dulness or convulsions in the initial period or at the time of the rash, especially in children under one year of age. Severe inflammatory changes though fortunately rare may even occur in the brain and its membranes. Considering the tendency to tuberculous new formations in association with measles, as has already been mentioned, the development of meningitis is to be feared. It may arise even after an interval of one month, but the other forms of meningitis, encephalitis, and poliomyelitis are much less frequent.

The bones and joints are but seldom involved, and here again it is chiefly a tuberculous process that is to be considered. Rheumatic affections which are so frequently observed with scarlet fever are here of rare occurrence.

Diagnosis.—As a rule the recognition of measles presents no difficulty provided that the disease follows the stereotyped course, especially in the appearance of the rash. Difficulty can arise in the prodromal stage in the absence of any trace of rash. The existence of an epidemic, the points noted in the history, and suspicious early symptoms, such as attacks of sneezing, snuffling, coughing, conjunctivitis, and slight rise of temperature are presumptive as to the onset of measles. This is made a certainty when Koplik's spots or red patches are visible on the mucous membrane of the cheeks or gums. The search for these must be continued for two or three days on account of their late appearance in some cases. The Koplik spots are the most important diagnostic signs in the early stage. They are best seen by diffused daylight, less distinctly by a glaring illumination such as direct sunlight or lamplight, on account of the lustre of the mucous membrane. Inflammation of the cheek, or particles of milk in young children, can give rise to error. These latter can be wiped away, and moreover the microscopic examination would show the existence of oil globules or fungi. Desquamation of the epithelium of the buccal mucosa and gums can likewise give rise to mistakes, but the greater extent of these flakes and their occurrence mainly on the gums, make a differentiation from Koplik's spots less difficult even though they are on the mucous membrane of the cheek, and at the same time not as white in color. In German measles, sometimes punctiform papules as large as of the head of a pin are scattered on the mucosa of the cheek which at first sight resemble the Koplik spots, but they are distinguished from them by their regular rounded form, their sharp margins, their pale red color, and the deficiency in the centre, distinctly bluish white in color, the result of epithelial necrosis. In favor of measles, on the contrary, the Koplik spots, when they are present, are an excellent differentiating point, as they occur in the majority of cases of measles and are wanting mostly in slight cases, and then particularly in the first year of life.

The eruption of measles like any other erythema causes great dif-

ficulty in diagnosis when it is less well defined and rudimentary in character, and not accompanied by fever. The differentiation from well-marked German measles, more than anything else, proves an obstacle to diagnosis which from a clinical standpoint cannot be absolutely obviated. These can only surely be distinguished early in the case when on the one hand the Koplik spots, and on the other, the small round spots typical of the early German measles can solve the problem as to diagnosis. The more intense forms of measles rash can lead to confusion with other erythemata. I have met with one such case in which there was marked infiltration of the individual spots, they were of a nodular form, livid red in appearance, and particularly as they stood in thick groups together, several of my colleagues made the diagnosis of variola. A glance into the mouth suffices as a rule to correct the error, quite apart from the other points of diagnosis (in measles, the preceding catarrhal signs, and the intense redness of the spots, in variola, a less thickly set papular eruption, oftentimes leaving the abdomen free, and with an early outbreak of pox upon the face, etc).

From *scarlet fever* the initial symptoms of measles are distinguished by the greater affection of the alimentary tract in the former, the greater angina, and the form of the rash. The region of the lips and chin is regularly free from rash in scarlet fever. An error in regard to scarlet fever can arise with the so-called confluent measles, yet in the general grouping together of all the symptoms, and the scrutiny of all the parts affected by the rash one will soon find some point or another characteristic of measles. Measles and scarlet fever may however occur together, and then they form a difficult diagnostic puzzle.

Serum rashes must be mentioned in conjunction with that of measles as they can show a great similarity in the skin and mucous membranes. The absence of the Koplik spots, the irregularity in the outbreak of the rash, also the sequence in which the several parts of the skin are affected, and above all the fact of the injection of the serum, will overcome the difficulty as to diagnosis. I have twice seen intense large typhoid roseola spots which had a great similarity to measles.

Difficulty may perhaps also arise with the maculopapular eruptions which occur with the gastro-intestinal disturbances of nursing infants, especially when they break out with great severity. These are intensely red, sharply defined, and quite isolated spots about the size of a bean; they occur mostly on the extremities, and are, like many artificially produced erythemata, characterized by the absence of any change whatsoever in the mucous membranes. Infectious erythema (see Plate 18) as well as erythema multiforme, is characterized by its diverse gyrate outline, its pale central portions, its localized occurrence especially upon the extensor surfaces of the extremities. A confusion of urticarial wheals with measles, is easily avoided.

a

a. Koplik's spots in measles.

b

b. Necrotic tonsillitis in scarlet fever.

c

c. Scarlet fever angina with diphtheritic-like membrane; raspberry tongue.

Prognosis.—This is usually good in strong healthy persons living in good hygienic conditions, even if the attack be severe and the general condition much affected. When the rash fades rapidly it is a threatening-sign; this applies to the adult, but still more so to the child. The mortality in private practice is very small. In Heubner's polyclinic in Leipzig it was 3.1 per cent. Jurgensen in Tübingen gives an average of 6.1 per cent. for 20 years. The mortality rates in hospitals alone are not to be compared, as here the death rate is frightfully high, and in many instances exceeds 30 per cent. This is not to be wondered at when one considers that only the poorest people send their children with measles to the hospital. These poorly nourished, anæmic and oftentimes tuberculous children, form with those already in the hospital, and secondarily affected with measles, the sure prey of death. That form designated as "Septic Measles" always leads to a fatal issue. By reason of the frequency of complications in the respiratory tract, children under one year of age furnish the greatest mortality. In one epidemic, Henoch gives the mortality rate under two years of age as $55\frac{1}{3}$ per cent.

Those rare measles rashes which break out with very high fever and severe general symptoms in the early stages, and which are often recognized only with difficulty, are unfavorable from a prognostic standpoint. The livid or brownish discoloration of the rash is to be interpreted as pointing to the onset of heart or lung complications, and is likewise unfavorable. Again, as to prognosis, as was formerly pointed out, the temperature is worthy of note when it does not fall to normal as the rash fades; this generally signifies the advent of complications. Of all the complications that can occur, mixed infection with diphtheria or influenza is the most unfavorable, as it appears that those infected with measles show a very much lowered resistance by reason of the lessened production of antibodies. A most frequent and unfavorable effect results from the advent of severe bronchitis and foci of pneumonia, and in consequence of existing or subsequent tuberculosis in predisposed individuals, likewise in rachitic, anæmic and weakly children, particular caution is enjoined in predicting the further course of the disease. The tuberculous lesions mostly arise after an interval of weeks or months of apparent well-being. Likewise one finds an increase of the hæmorrhagic diathesis in those formerly predisposed to it. While purpuric conditions following measles are seldom of unfavorable prognosis, hæmophiliacs show during measles grave progress in their constitutional anomaly. We may be easily enticed into an unfavorable judgment of the course of the disease by the condition of the nervous system, as by convulsions, delirium and stupor. These in all their severity, so long as they do not last many days, are of no permanent harm, as they are of an evanescent nature, and are not to be interpreted as of bad prognosis.

Of the intestinal disturbances, only the severe dysenteric lesions are to be feared as dangerous to life. The early intestinal disturbances are mostly slight and of short duration.

Prophylaxis.—By reason of the easy transmission of measles in the early stages, precautionary measures to prevent the infection often come too late, and the children who are thus carefully isolated from the patient, share one after another the lot of their companions, unless they possess a high grade of immunity against measles and that is rare. On this account in many of the villages of Southern Germany the custom prevails of intentionally putting the children who have not had the disease into houses where measles exists, so that by close contact they may contract it as soon as possible, since it is regarded as inevitable and so little to be feared. Separation of the members of the family from those who have measles may be regarded as useless, unless it is done at the very onset of the initial stage (*i.e.*, beginning of Koplik spots) and therefore after a very short exposure. On the other hand it is well to take precautions against the extension of the disease to other communities, as measles is transmitted over great distances with great difficulty, if at all. School physicians together with the teachers, are called upon, especially at the time when respiratory catarrh is prevalent, (considering the predisposition to measles), to take precautionary measures by timely inspection, in the earliest stage of disease, to protect the children who are still unaffected as well as the rest of the community. This is to be accomplished by immediate inspection from house to house, and by the closing of the schools.

The child who has had measles should remain away from school for at least three weeks from the beginning of the illness. This applies also to the children of the family who have been exposed but not isolated. If these were immediately separated from the patient, and taken to another residence, sixteen days quarantine is sufficient before they return to school. Just as in the case of schools, so may other gatherings of young persons during an epidemic serve as the origin of infection, such as at children's parties, play grounds, games, etc. The anxiety as to a second attack is usually not justifiable when the first attack was surely measles. It can, however, certainly occur, but it is very rare.

It is well to shield from measles, children under three years of age, those that are weakly, those predisposed to catarrhal affections, those whose brothers and sisters have died from tuberculous meningitis, and those predisposed to tuberculosis, or who have already suffered from it, or from hæmorrhages or any other malady. Existing chicken-pox and whooping-cough are said to produce a heightened susceptibility to measles though personally I have not as yet observed it.

If the disease is in the incubation or prodromal stage the child is to be protected from taking cold, which will at any rate have a therapeutic

effect. In the stage of incubation the child may be carefully taken into the fresh air, but in the prodromal stage, the bed is recommended. Special care for fear of taking cold (pseudocroup, pneumonia), is necessary when the prodromal period is protracted.

Cleanliness and other hygienic rules are the most important prophylactic measures during and after the illness. The sick room should accordingly have dry walls, and contain the purest possible air, should be large and bright, not situated on the ground floor, and should have windows opening to the south or west. The temperature should range from 15°–16° C. (57°–60° F.) the moisture of the air must be controlled, for we know that with measles in unhygienic and badly-ventilated rooms with deficient change of air, affections of the respiratory tract much more often develop, and run a relatively more severe course. Frequent change of body and bed linen, previously warmed, is advisable, and the bed clothes should retain the heat well, but should not be too heavy. The daily bathing of the face and hands with lukewarm water is regularly to be carried out. The care of the mouth several times a day is necessary and proper, for this in itself may obviate the occurrence of the various affections likely to arise during the disease. I mention these hygienic rules, which speak for themselves, because it is found that even in the better and more intelligent classes of the community a real fear exists regarding the washing of the patient and the changing of his garments.

In order to guard against the frequent intestinal disturbances, it is well during the disease to enforce a rigid diet, and strongly forbid all indigestible foods, such as breads made with yeast, raw fruit, etc., as well as unnecessary drinks.

By reason of the tendency to necrosis of the tissues, every form of trauma, be it mechanical or thermal, is to be absolutely avoided.

If the period of convalescence has run for eight days without fever or cough, and the patient's strength has sufficiently recovered he may be permitted to leave his bed. Care must be taken after measles on account of the lowered resistance, especially of the respiratory tract, and the patient should not leave his room for another eight days at least during the colder periods of the year. The association with other children, as before stated, may be permitted for the first time after the close of the period of convalescence, on the one hand, on account of the ready transmission of the disease to them, and on the other, because of the danger of the exposure of the patient to some other disease. Particular care should be taken to avoid exposure to diphtheria and whooping-cough to which those convalescing from measles are known to be very susceptible. It goes without saying that one should prevent for a long time any one affected with tuberculosis from having any contact with a person that has recently had measles, and on the other hand, a measles

patient is so disposed to tuberculosis that he can be said to be safe from danger of tuberculous complications only after months of observation.

The disinfection of the sick room in uncomplicated measles is an unnecessary procedure, considering the slight tenacity of the measles virus. Filatow's suggestion that a two or three days' airing of the room is preferable to troublesome disinfection measures, is commendable.

Treatment.—Aside from the prophylactic measures which form the most important part in ordinary cases, and in the absence of a specific therapy, the treatment of measles is limited to the combating of individual symptoms, and the regulation of the diet.

In order to lessen the intensity of the conjunctivitis it is well to let the patient wear eye shades, or the sick room may be darkened. I have not been able to observe any more favorable effect on the course of the disease by the exclusive use of red illumination by means of curtains or glass of that color. For the severe attacks, one can advise from time to time during the day, washing the *eyes* with boiled lukewarm water, or 2 per cent. boracic acid solution. The purulent crusts adhering to the eyelids are best removed by smearing with lukewarm almond oil. Should phlyctænulæ develop they are best treated with 1 per cent. yellow oxide of mercury ointment or dusting with calomel. Applications of 1–2 per cent. solutions of blue stone produce a very intense catarrhal inflammatory process. Ice poultices are not to be recommended. The neighboring skin of the lids may be protected from maceration by the tears, and resulting eczema, by frequent smearing with vaseline or lanolin. Diphtheria of the eyes is combated by serum therapy (3000–6000 units) and applications of bichloride of mercury 1:5000.

The *coryza*, and particularly the troublesome sneezing is modified, and may even be cured by frequent instillations of oil, or 1–3 per cent. borovaseline into the nose. For very severe nasal catarrh, one may, two to three times a day, introduce alternately into the nostrils small tampons of cotton soaked with 1 per cent. cocain solution and as soon as the passage is pervious, oil or vaseline or 2 per cent. yellow precipitate ointment may be freely used. For epistaxis, it is sufficient to snuff up some acetic acid and water, and if the hæmorrhage be greater a small tampon may be introduced alone, or, soaked in a solution of adrenalin, it is sure to succeed. For severe nasal diphtheria, besides free serum therapy, careful syringing of the nose with 2 per cent. solution of boracic acid is recommended to prevent the formation of membrane. The favorite procedure of blowing boracic acid and other powders into the nose is not to be advised, on account of the irritation of the mucous membrane which they produce, the same applies to the preparations of menthol. The skin about the nostrils must be protected from the irritating discharges by the application of glycerin, lanolin, etc., the

greatest care is necessary in the cleansing of the nose, and with it a frequent change of handkerchiefs.

For catarrhal *otitis media* diaphoresis is to be produced by hot drinks or sodium salicylate, 0.25–2.0 Gm. (4–30 gr.), aspirin, 0.15–0.5 Gm. (2–7 gr.) at a dose are recommended, possibly warm solutions of dilute acetic acid to the affected ear may hasten the absorption of the exudate. In this as in the purulent form, the severe pain will be alleviated by the instillation of 5 per cent. carbol-glycerin. In case, however, this does not suffice it is necessary on account of persistent high fever and the accumulation of pus to puncture the drum-head. In very young children (nursing infants) this may be delayed, as the pus readily escapes spontaneously, and moreover the field of operation is small and unfavorable. The purulent discharge from the ear is best combated by the use of peroxide of hydrogen and distilled water equal parts, and if the pus be very offensive and thick, careful irrigation with a weak solution of potassium permanganate, creolin, or boracic acid is permissible. If the radical operation is necessary, let it be done early, as soon as the purulent process extends to the mastoid antrum. The after-treatment is tedious but it gives excellent results.

The *care of the mouth* as already mentioned requires special attention. The troublesome dryness of the mouth in young children may be overcome by frequently giving boiled water, tea, etc., or by carefully spraying the mouth with water. In older children gargling with refreshing washes relieves this dryness, or when greater pain is present with marshmallow or sage tea. The development of aphthæ is treated by a carefully arranged nonirritating diet, also by frequent painting with a solution of 1–3 per cent. aneson, or a solution of copper sulphate, and eventually by touching the lesions with a bluestone pencil. Internally one may prescribe silver nitrate (1 to 1000) a teaspoonful at a time in severe and uncontrollable cases (for instance in the case of small unmanageable children) (metal spoons must not be used). A 1 per cent. solution of potassium chlorate may be used with success as a gargle in aphthous stomatitis (this may be used internally in a solution of 2 to 5 grains to the ounce of water).

Noma, which is rare, should be removed by the cautery or excision. The frightful odor emanating from it can be controlled most readily by dusting pure wood charcoal powder over the gangrenous parts, this may be used alone, or combined with equal parts of dermatol with the addition of five or six drops of oil of cade. An application or wash with a 2 per cent. solution of antinosin is also recommended.

Should diphtheritic deposits appear in the mouth, antitoxin should be administered as speedily as possible; the same applies of course in a still greater degree if the process extend to the larynx. As before stated, one must constantly keep in mind the fact of the greater predisposition

to *diphtheria* exhibited by those who have suffered from measles, the particularly great loss of antibodies to diphtheria demands a more liberal administration of antitoxin, 5000 to 6000 units is to be the initial dose in undoubted diphtheritic croup, energetic treatment it is true, but nevertheless correct. As a further therapeutic procedure we think that the immunization of all the measles patients in the hospital (by the injection of 200 or 300 units of antitoxin) is to be recommended, the danger of infection in such patients lasts for several weeks, and it is indeed a great one, so that possibly the immunization may be repeated at intervals of say 14 days in spite of the unpleasant effects that may arise from such reinoculation. The treatment of diphtheria with measles differs from that generally followed in that it must be remembered that diphtheritic croup in the first place gives rise more readily to the development of foci of pneumonia, and in the second place that it much more frequently extends far downwards as a descending croup. Heart tonics, above all infusion of digitalis, 0.15–0.5 Gm. to 70.0 Gm. (2–7 gr. to 2½ oz.), caffeine sodium benzoate, 0.1–0.3 Gm. (1½–4½ gr.) given daily internally or subcutaneously as well as the usual expectorants will often overcome the first-named danger. As to the operative treatment of diphtheria with measles, in opposition to the usual course, I would give preference to primary tracheotomy, and only in the very lightest cases of croup, would when necessary, suggest intubation, the frequent simultaneous pneumonic complications, the tendency of the croup to descend, and the greater vulnerability of the mucous membrane, and, as a result the greater danger of ulceration are my main reasons for this.

Subglottic laryngitis or pseudocroup in the prodromal stage of measles presents no difficulty in the treatment, as it usually disappears spontaneously after the outbreak of the rash, moderate diaphoresis, frequent administration of warm drinks (tea, lemonade), inhalations with steam atomizers, expectorants, very hot poultices over the throat, or the inunction of mercurial ointment suffice. Counterirritants such as mustard, or one or two leeches over the larynx may be used in the more severe forms, such as may come on in the exanthem or convalescent stages. In pseudocroup also, in spite of all, the question of tracheotomy or intubation must be discussed and the decision as to which is preferable has to be made. Usually here intubation is to be preferred particularly in view of the brevity of the affection.

The *bronchitis* of the early stages of the illness is often troublesome and is usually the expression of the rash on the bronchial mucosa, which the bronchitis causes to disappear. It is always imperative to ventilate the room, and that the patient be not harmed by doing so (as by draught). It is further necessary to modify the attacks of coughing with small doses of codeine. Expectorants are not called for in the dry

form of bronchitis, where there is much secretion as in capillary bronchitis or in the closing stage of pneumonia. Ipecac or some other expectorant, will render good service.

With pneumonia or failing heart it is well to employ heart tonics early, such as infusion of digitalis, caffeine, the tincture of strophanthus, or injections of camphorated oil may be tried. If there be much lassitude and prostration alcohol must be used. Of course this can be administered only in moderate quantities, either cognac or Malaga wine mixed with other fluids may be given to nursing infants drop by drop or to older children by the teaspoonful at a time. It is also well to administer a light white wine in the form of a wine soup. It is quite inexcusable on the grounds of temperance to exclude alcohol, that great saver of tissue waste, from the physician's armamentarium, even if its efficacy is accomplished only at the cost of inhibiting the action of the vagus nerve. The harmful effects of alcohol, as with any other medicines, arise only from the long continued consumption of large quantities.

The nausea produced by medication, as often formerly occurred for instance in capillary bronchitis or in the closing stage of pneumonia, should on account of the heart always be avoided with the utmost caution.

An important part of the treatment in the bronchitis and pneumonia of measles is *hydrotherapy*. As to whether this form of treatment can cut short, or form a barrier to the disease is very doubtful.

The changes in the rash (livid discoloration and washed out appearance) already spoken of, such as often appear in the course of severe heart and lung complications, and called by the laity "relapsing measles," the popular mind readily ascribes to the hydrotherapy. Unfortunately at times the lung conditions increase, in spite of scientific treatment mostly however it is where the activity of the heart and the general condition have been overlooked, and even the most serious symptoms (as for instances cyanosis of the mucous membranes and the peripheral parts of the body as well as coldness) remain unnoticed.

A cool pack to the nape of the neck (a towel wrung out of water at 25° to 28° C. (77° to 82° F.) and covered with a larger bath towel), may in many cases not only reduce the temperature, but by it the general condition may be improved, and pain and difficulty in breathing alleviated. By three applications at intervals of twenty minutes a favorable lowering of temperature will readily be obtained, whilst in other cases, where the fever is not so high, but the other symptoms are troublesome, a longer continuance of the applications (two to four hours) is desirable. When these are to be frequently repeated a previous anointing the skin of the part is well as a preventative against eczema. If dyspnœa and prostration increase and there be deficient expectoration, warm baths (35° C.; 95° F.) with a cooler douche, carefully

used, are often beneficial. Hyperæmia and diaphoresis, and thereby a relatively greater radiation of heat from the skin can be increased by mustard baths (50–100 Gm. per bath) or as Heubner suggests, by wrapping in mustard water (½ kilogram to 1½ litres of warm water). While these means are employed in weakly and reduced children, I should advocate blood letting in the form of leeches or venesection where one has to deal with strong well nourished children, in preference to all other methods.

The inhalation of oxygen, in many cases, especially in severe bronchitis, brings about an improvement of the subjective symptoms and a lessening of the respiratory frequency.

The *tuberculous affections* of the respiratory tract, glands, brain and skin, etc., must be combated by sufficient nourishment under favorable climatic and hygienic conditions, with mental and physical rest. Creosote and its derivatives may be administered in moderate quantities. With local tuberculous processes iodine and the inunction treatment are to be employed before the time for surgical interference. For the simple inflammatory adenitis the application of moist warm poultices of five to ten per cent. of ichthyol ointment are successful.

For the *intestinal catarrh*, a restricted diet is sufficient for a cure at the beginning of the disease and yet will sustain the patient during the febrile period with his loss of appetite. Apart from dietetic measures the later severe colitis is combated by frequent irrigations with warm boiled water at 40° C. (104° F.) either alone, or with the addition of tannin 1 per cent. or acetic alum 1 to 2 per cent. or with 50–100 c.c. of 1 per cent. silver nitrate solution, likewise by giving the bismuth preparations by mouth. If bacteriologically Kruse dysentery be diagnosed one must not hesitate in the administration of a corresponding serum. Much may be done in a prophylactic way to prevent these intestinal troubles, if from the onset of the disease undue irritation of the intestinal mucosa is avoided by a sensible and not an immoderate administration of medicines (digitalis and alcohol, etc.), and a light diet. The diet should be mainly liquid (tea, soup, milk, cocoa), which may with improving appetite be changed to soft easily digested foods, (sago, tapioca, and eventually minced meat).

The *nervous symptoms*, as dulness, convulsions, delirium, headache and jactitations are to be treated by cold applications to the head or general wet packs at a temperature of 27° C. (80° F.) mustard packs or mustard baths, likewise the administration of sodium bromide, 0.15 to 1.0 Gm. (2 to 15 gr.) or pyramidon, 0.1 Gm. (1½ gr.) may be tried. In emergencies, when the cerebral signs do not abate, spinal puncture is highly recommended as a means of relieving the brain of the over accumulation of cerebrospinal fluid. Prostration and the pains in the limbs can be relieved by the limited administration of alcohol (Malaga

wine, cognac), also by rubbing with dilute acetic acid or some alcoholic solution, and internally some sodium salicylate or aspirin.

Sharp rise of temperature the result of measles and its complications is best influenced as already stated by hydrotherapeutic measures. Where these are unsuccessful small doses of aspirin, quinine or aristochin may be given.

Sometimes there is irritation of the skin, which is best relieved by sponging the parts with diluted alcohol or by the use of salicylic acid or menthol, also by some protective covering such as oil or a dusting powder. Sponging is preferred particularly if there is desquamation of the skin at the time.

The eczema and other skin changes following measles require efficient treatment which need not be discussed here.

At the end of the attack of measles and its associated troubles the patient should take particular care of the skin by taking one or two full warm baths before leaving bed. The patient may leave his bed eight days after the subsidence of the fever, generally after another eight days he may be allowed to go out of doors, but the time of year and the state of the weather will decide this.

SCARLET FEVER

BY

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TRANSLATED BY

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IT is true that the clinical picture of scarlet fever has been well known for many centuries, but not until the end of the seventeenth century did Sydenham, who studied the great epidemic of London, in 1661–1675, give a clear-cut description of this affection. He designated the disease scarlet fever and differentiated it definitely from the other exanthemata of infectious origin. Since then scarlet fever has been met with in nearly all countries, and among all peoples, sometimes so mild in its manifestations as to go unrecognized and lead to therapeutic errors, at other times of such a malignant nature as to terrorize. Until quite recently Japan was almost immune to this disease. English authorities ascribed this to the absence of a free use of milk. Since the Russo-Japanese War—as Japanese physicians hold—scarlet fever is met with frequently in Japan.

A marked advance in the study of scarlet fever was the clinical and bacteriologic differentiation made between scarlatinal angina and true diphtheria.

ETIOLOGY AND PATHOGENESIS

The exciting cause of scarlet fever has not yet been determined definitely. That the disease is of protozoon origin is a belief steadily gaining strength. Sponsors for this theory are Mallory, Duval, Siegel, Prowazek and Gamoleia. Mallory found the "Cyklasterion scarlatinale" in sections of the skin. Duval found these same bodies in the fluid of blisters artificially produced by means of ammonia. Rach and I have repeated Duval's work and can confirm his findings. Field, however, described similar findings as occurring in other conditions, thus casting some doubt on the correctness of Mallory's observations and making further study and investigation necessary. Similarly, the findings of Gamoleia (Chrysantozoon scarlatinæ) lack confirmation.

It is a well-known fact that often after death from scarlet fever streptococci (according to Moser, in 60 per cent. of the cases) are found in pure culture in the throat, in all suppurative processes (lymph-nodes, ear), in the viscera, and in the blood. During life Jochmann succeeded in finding them only occasionally (21 times in 121 cases), and then only in fatal cases. Meyer, however, found streptococci in the less severe cases and such as terminated in recovery.

The majority of observers are of the opinion that this streptococcic invasion must be regarded as being secondary to an infection by some other as yet unknown organism. Others, however, consider them as being the exciting cause of the disease. They hold that the streptococcus scarlatinus represents a specific strain of coccus, which resembles other streptococci (erysipelas, puerperal fever, etc.) only morphologically. The chain of evidence is not yet complete because up to the present time it has been impossible to produce a scarlatinal infection, either in man or in animals, by means of pure cultures of the streptococcus. The endeavor to establish a relationship by means of complement binding or agglutinating substances in the blood serum has likewise failed.

Russian observers (Gabritschewsky and his scholars) have directed their efforts toward experimentally producing an abortive type of scarlet fever, with dead streptococci (streptococcus vaccines), and thus effect an active immunity, but thus far they have failed. It is worthy of note in this connection to recall that so far as streptococci are concerned, findings similar to those obtained in scarlet fever have also been noted in other infections, such as plague and variola. Furthermore, the fact that an attack of scarlet fever confers immunity is put forward as evidence against the streptococcic nature of this disease, because in other streptococcus infections, such as erysipelas, an increased susceptibility to such infection is known to follow recovery.

However, regardless of any etiologic relationship that streptococci may have with scarlet fever, it is generally admitted by all observers that the course of the disease is materially influenced and the welfare of the patient correspondingly threatened by these various streptococcus infections occurring in the course of scarlet fever.

So far as the virulence of the exciting cause of the disease, whatever that may be, is concerned, in none does the "genius epidemicus" play so large a rôle as in scarlet fever. In some epidemics the nature of the disease is an extremely mild one, with little or no mortality, while in others from thirty to fifty per cent. of the cases terminate fatally.

The portal of entrance of the exciting cause is problematical. Inasmuch as the first or initial symptom of the disease is usually redness and swelling of the pharynx, it is generally assumed that it is here that the infection takes its origin, and that, therefore, the pharyngeal affection is to be regarded as the primary one. Although the correctness of this assumption can only be proved by the discovery of the causative organism, many of the findings point in that direction, especially the occurrence of scarlet fever in wounds, and following burns. In such cases the exciting cause of scarlet fever evidently enters the body by some route other than the pharyngeal. It is to these atypical cases that the term "extrabuccal" scarlet fever is applied.

It is somewhat difficult to determine the length of the incubation period—the time intervening between the occurrence of the infection and the appearance of the first or initial symptom. Its variability is characteristic of scarlet fever. Furthermore, even when infection has occurred, the disease itself may not follow.

Paula N., aged 2½ years, wrongly transferred to a scarlet fever station, did not show any evidence of the disease until the twenty-second day.

Only a minimum incubation period of less than twenty-four hours can positively be determined (Trousseau, Sôrensen). This can easily be observed in the case of house infections occurring in tracheotomized patients. The average incubation period is from three to five days.

One attack of scarlet fever usually confers life-long immunity, but second attacks have occasionally been observed.

Theresia H. First attack occurred at the age of three years. Typical angina and unquestionable desquamation. Dismissed from the hospital, January 23, 1898. Readmitted with a second attack April 2, 1902. Highest temperature recorded during this attack, 38.8° C., on the second day. Recurrence by lysis. Temperature normal on the tenth day. Desquamation.

The infrequency of such second attacks of scarlet fever is in marked contrast to diphtheria, where such an occurrence is relatively frequent, even within a few months after recovery from the first attack.

The existence of a natural immunity or an inborn resistance to scarlet fever can not be established, but it is true that only a comparatively small number of children exposed to the infection become ill, and adults only exceptionally. Certain it is, then, that the resistance to infection in the case of scarlet fever becomes greater with the advance in years. Family predisposition can not be considered in this connection, because, while in some instances all the members of one family are stricken simultaneously, in the greater number of cases only one child becomes ill, or many children suffer from other and various diseases.

It is impossible to state whether family predisposition can be considered a prominent factor when all members of a family are similarly affected or whether it is an evidence of the genius epidemicus.

Three children acquired mild scarlet fever. Lymphadenitis and subsequent nephritis were noted at about the eighteenth day (18, 18, 19); even the course of the nephritis was the same in all three cases; the urine was albumin-free on the thirty-second, thirty-second and thirty-fourth day.

The greatest susceptibility to the disease is noted in the first decade of life, between the ages of three and eight; during the first six months of life resistance to scarlet fever is almost absolute. Diphtheria and whooping-cough, on the other hand, may occur during the first few months of life. The resistance of adults is by no means absolute; the

infection may gain a foothold, especially when an increased predisposition has been established by a previous pharyngeal trouble, particularly diphtheria.

Dr. v. P. was on duty in the scarlet fever pavilion from December 1, 1901, to February 1, 1902, and did not contract the disease. Toward the end of March he had a mild attack of diphtheria, returning to duty March 27, 1902, with his pharynx still inflamed. April 5, 1902, yellowish-gray spots were noted at the posterior pharyngeal wall, and on the hard palate anteriorly. On the following day he presented the typical scarlet fever eruption.

I have seen two exactly similar cases in the past two years.

I have already referred to the fact that scarlatinal infection may and does occur at the site of wounds, injuries of various kinds, especially burns (Leiner); in fact, there is noted at such times a peculiar predisposition to infection. The same is true during the puerperium.

Occasionally the reason for the occurrence of scarlet fever can not be determined.

For instance, Johanna R. became ill with scarlet fever after being on duty as nurse in the scarlet fever pavilion only two days.

The relationship of this disease to a diminishing predisposition is vastly different from what occurs in the case of measles, where, irrespective of the age of the individual, infection occurs at the first exposure. The onset of these two diseases in epidemic form in closed institutions is also distinctive. In the case of measles many cases occur at one time and the epidemic outbreak terminates rapidly. In the case of scarlet fever, on the other hand, the number of cases rises steadily, and sporadic cases occur for a long time afterward.

That brings us to the question of the method of infection. In the case of measles, there is usually a history of direct contact with a measles patient, either in the prodromal or the eruptive stage of the disease. Infection by indirect means, such as an intermediary, animate or inanimate, is the exception. This may be taken to indicate fairly conclusively that the exciting cause of measles is short-lived; that is, its infectivity is of exceedingly limited duration.

The opposite is true of scarlet fever. Beyond question the virus is conveyed from one person to another by means of the desquamation, the clothing of the sick, and through the agency of a third person. It is not possible to state whether the desquamating epidermis is infective of itself or only when it serves as a carrier for the secretions (ear, mouth). Stickler proved the infectivity of the pharyngeal mucus. He succeeded in infecting twelve well children by injecting pharyngeal mucus subcutaneously. The virulence of the scarlet fever virus remains undiminished for years. Numerous instances in the literature in support of this statement can be cited.

The conditions existing in Vienna are hardly such as permit of investigations on this point. Scarlet fever is endemic, cases are met with at all times, and one can not, therefore, with any certainty, exclude unusual methods and sources of infection. The following case is an apt illustration, occurring, as it did, in a locality absolutely free from scarlet fever in epidemic form:

Rosa B. had scarlet fever at the age of four and a half years. She was taken to the hospital and succumbed to the infection. Her clothing was disinfected thoroughly, except a fur coat and cap and a pair of shoes, which the mother feared might be ruined by the disinfection. These articles were kept in a box in the attic of her home for two years, when a sister of the deceased patient was able to wear them. Four days after the little girl first donned this clothing she became ill with a moderately severe case of scarlet fever.

As a matter of fact, probably only a small percentage of cases are of such origin, but these cases do occur. As a rule, infection occurs only by direct contact with the patient, even in scarlatina sine eruptione, the anginose form. At which stage of the disease infection is most apt to occur can not be determined. However, in the so-called house infections it has been demonstrated that in most instances it is possible to prevent a spread of the disease to bed neighbors if the patient is isolated on the first day of the eruption. It is hardly probable, therefore, that there is any danger of infection during the incubation period (Vogl).

One of the most distressing things in connection with scarlet fever is the fact that by no known means can it be determined for how long a time the patient remains a source of infection. We have observed a number of instances in which children, even after a six or eight weeks' stay in a hospital, numerous baths and disinfection of their clothing, returned home and promptly infected other children of the family.

Marie S., twelve years old. Mild attack of scarlet fever. Discharged on fortieth day; no desquamation. This was on December 11th. Three days later, December 14th, Gisela, thirteen years old, December 18th, Margaret, four years old, and December 23d, Albert, six years old, gave evidence of a mild scarlatinal infection.

Whether the infective virus is contained in the secretions (nose, mouth, ears) or in the dust of the ward, which is carried away on the body and clothing, is a moot question.

GENERAL SYMPTOMATOLOGY

The onset of the disease is usually sudden. It is characterized by vomiting, sore throat, fever and a general feeling of malaise. The child is perfectly well in the morning, goes to school as usual, and is suddenly taken violently ill during the session. One of the resident physicians in our scarlet fever hospital was stricken suddenly while on his rounds, having till then enjoyed the best of health.

To attempt to distinguish a prodromal stage is useless; the first evidences or manifestations of illness should be designated "initial symptoms."

If, perchance, the patient is seen shortly after the appearance of these initial symptoms, it will be noted that besides the elevation of temperature and the lassitude, the face is puffy and red. The conjunctivæ and nasal mucous membrane are normal (unlike measles), but the mucous membrane of the cheek and gums is slightly reddened and thick, the dorsum of the tongue is heavily coated and discolored. The depth of color increases from before backward, the palate, hard and soft, and the uvula being blood-red. The tonsils are red and swollen, and even as soon as this lacunar deposits may be seen. The paratonsillar lymph-nodes at the angle of the jaw are enlarged and tender to touch. The heart action is conspicuously increased in frequency.

The further progress of the disease is a rapid one. The temperature rises quickly; a temperature of from 39° to 40° C. (102° to 104° F.) is by no means infrequent. In the course of a few hours the typical scarlet red, miliary eruption of scarlet fever makes its appearance. The lesions are from two to three millimetres in diameter, somewhat circumscribed, not elevated appreciably above the skin surface, forming a mosaic pattern, appearing first on the upper part of the trunk, and then spreading rapidly over the remainder of the trunk. In a little while it makes its appearance as far down as the groin, with isolated outrunners on the inner side of the thigh. Backward, it extends as far as the hips, ending in a triangular border, the tip of the triangle pointing toward the sacrum.

The cheeks are uniformly red, the eruption being confluent, and spreading over the bridge of the nose, as is seen in erysipelas. In contrast to the eruption of measles, the peri-oral region is free from eruption and presents a pale triangular section of skin, the base downward, presenting a sharp contrast to the otherwise general redness of the face.

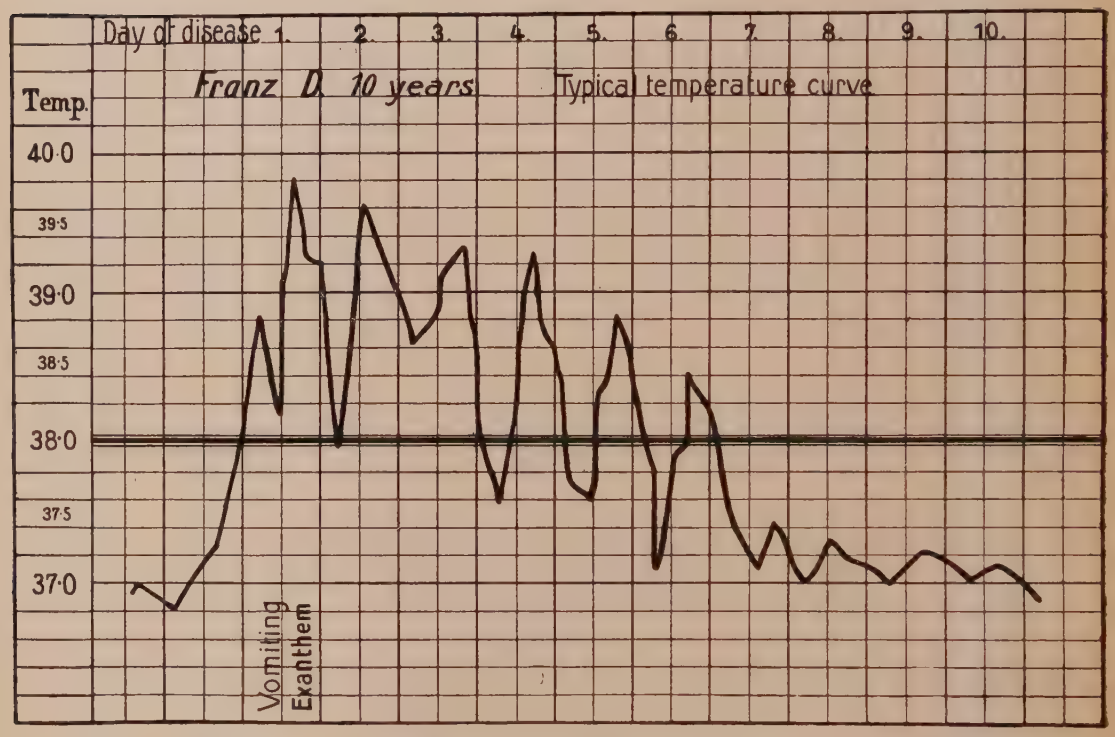
Subjectively, the lassitude, angina and headache are the symptoms complained of most. The patient desires to remain in bed, his appetite is lost, but, on the other hand, thirst is complained of bitterly. There is constipation and the urine is diminished in amount, high in specific gravity, but containing no pathologic substances until the appearance of the febrile albuminuria. In the milder cases the diazo-reaction is negative; peptone is increased in amount, although, as was pointed out by Tobeitz, this is not to be regarded as of any prognostic value.

If the disease made its appearance in the morning, the clinical picture is one as described above.

It is seldom indeed that the rash is delayed for twenty-four or forty-eight hours. If it makes its appearance later than this, one must take into consideration whether it was not possible that the scarlet fever is secondary to an ordinary angina.

The patient has a restless night and is often delirious. In the early morning hours the temperature falls somewhat, but the general condition of the patient remains unchanged; in fact, the angina often becomes more intense, the lymph-nodes at the angle of the jaw are much more sensitive to pressure, the rash now appears on the extremities and is much more extensive or more confluent on the trunk. The shoulder-girdle is more or less covered by the eruption, and it is also extending to the upper extremities as far as the lower third of the forearm, even the dorsal surface being involved. Finally, the rash spreads to the hand, the vola manus is diffusely reddened, the dorsum of the hand, especially

Fig. 48.



Typical temperature curve in scarlet fever.

the dorsum of the fingers, and the contiguous phalangeal surfaces present a flaky eruption and swollen follicles. The latter are also found on the trunk and extremities. The flexor surfaces of the upper extremities, from the middle of the upper arm to the lower third of the forearm, are usually only slightly involved, the eruption appearing here at a later time. On the lower extremities the eruption first makes its appearance on the inner side of the thighs and then on the remaining parts of the legs. The dorsum of the foot and the extensor surfaces of the toes likewise present the swollen follicles which appear on the backs of the hands.

Coincident with the increase in severity of the symptoms during the

PLATE 12.

Eruption of scarlet fever on the chest at the beginning of the eruption.

second day, the evening temperature becomes higher and the morning temperature is above normal (Fig. 49).

In uncomplicated cases the clinical picture is at its worst stage in from three to five days. The reddening and swelling of the pharynx has increased, and the mucous membrane of the mouth is diffusely reddened and swollen (enanthem analogous to the exanthem); the slimy yellowish coating on the tonsils has spread.

The macular eruption on the body has become more intense and a new crop has made its appearance among the older eruptions, so that in the more intense cases the skin now presents a diffuse redness when viewed from a distance. It is only when one looks more closely that it is seen that the eruption is still macular. The entire skin, especially the skin of the trunk and thighs, appears to be infiltrated, swollen and inflamed. The follicular swellings either remain unchanged or have also become more intense; very often they are converted on the third or fourth day of the disease into small papules filled with a cloudy, purulent fluid. These are the so-called "frieseln" of the Germans, or the type of eruption designated as scarlatina miliaris. The appearance of these papules is regarded as of favorable prognostic value.

Of rather unfavorable prognostic value are to be regarded those forms of the eruption which more nearly resemble the eruption of measles —a maculopapular eruption—which stands out in sharp contrast to the bright red eruption of the typical case of scarlet fever. This is especially noticeable when viewed from a distance. It is the so-called double exanthem, the *scarlatina variegata.*

The scarlet fever eruption disappears on finger pressure early in the disease, but on the lower portion of the trunk, especially the skin of the abdomen, the area of finger pressure anæmia is seen to be distinctly icteric in color. The reason for this discoloration is unknown, although beyond question this is not a typical icterus, because this is only rarely associated with scarlet fever. I have seen two such cases. When the skin is stroked with the finger-nail or with the point of some object, there appears in from one-quarter to one-half a minute a one centimetre wide anæmic line on either side of the stroke (*Raies blanches* of the French), the stroke itself remaining slightly reddened. This symptom is not observed in all cases; its intensity is extremely variable. In several very intense cases I have observed it as late as the middle of the second week of the disease.

Such portions of the skin surface as are exposed to pressure (axillary folds, elbow crease) often present punctiform ecchymotic spots. This is of no significance other than to indicate that the blood vessel walls have become more friable, of which one can easily convince himself by picking up the skin—preferably in the infraclavicular region—between thumb and forefinger and pressing it slightly for about five seconds. Even very slight pressure suffices to cause numerous punctiform hæmorrhages.

In the case of children with normal skin greater pressure is necessary to produce the same effect, although this finding is obtained in many hyperæmic conditions of the skin, especially in measles, although greater pressure must be exerted and even then the hæmorrhage is not as intense as in scarlet fever. Therefore, these hæmorrhages are not to be regarded as being of diagnostic value. Hecht attempted to measure the intensity of these skin hæmorrhages as produced by varying pressures, but his results were so extremely variable as to nullify the finding. These hæmorrhages are easily made to appear as late as the end of the first week of the disease.

A genuine purpura is seen but seldom, and then only late in the disease. It is probably caused by sepsis. I have seen only one such case, although several instances are recorded in the literature (Risel). This hæmorrhagic diathesis does not stand in relationship whatever to the ordinary hæmorrhages.

In the more intense cases the eruption remains at its height until the fourth or fifth day, appearing to be more red in the afternoon and evening than in the morning. From that time on it begins to pale in the same order as it made its appearance, first on the face, then on the trunk and extremities. The infiltration of the skin gradually disappears, the skin becomes dry and shrunken, brownish-yellow in color, and a distinct pigmentation is seen on finger pressure. This pigmentation is more diffuse and less intense than in the case of measles.

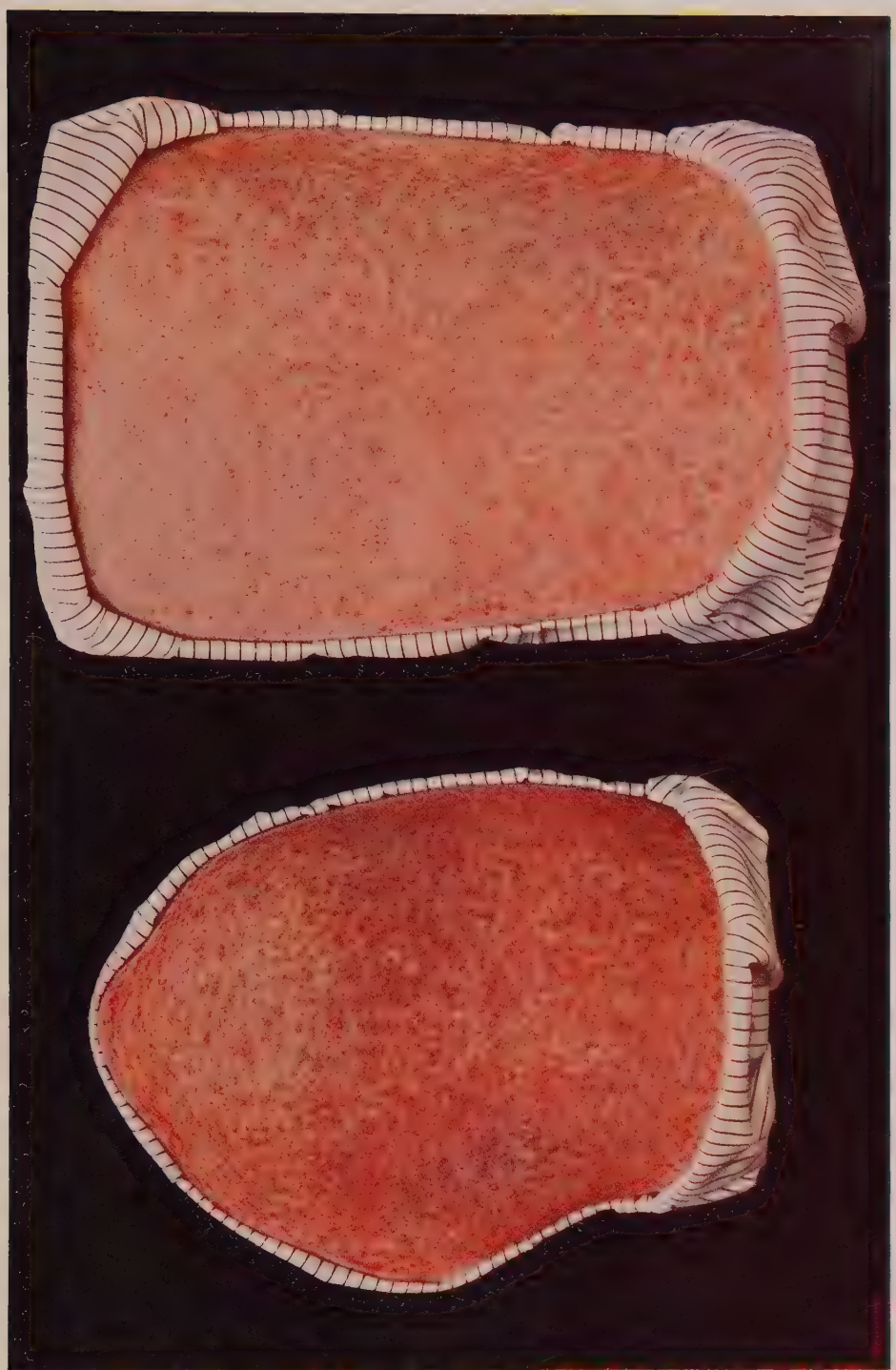
The redness and swelling of the pharynx and the eruption on the oral mucous membrane disappear slowly, the coating on the tongue gives way to a dark-red color, first at the tip, then gradually extending backward. It is still somewhat thickened and the papillæ are prominent (raspberry, strawberry or cat's tongue).

The lymph-nodes in the angle of the jaw diminish in size, are less tender to touch; the pulse becomes less frequent, the subjective symptoms disappear, the appetite is again keen, and the patient is more restful at night. Beginning with the third or fifth day, the temperature falls by lysis, the morning remissions go more nearly to normal, and the afternoon rise is less high. By the commencement or middle of the second week the temperature is again normal (Figs. 48 and 49). This decline of the temperature by lysis is so characteristic of scarlet fever that any departure therefrom must be noted carefully and the reasons therefor ascertained.

It is of interest to observe that when in the course of this fever curve an afternoon rise occurs, such rise, even in the favorable cases, marks the appearance of a new lysis, and the fall to normal is correspondingly delayed.

A crisis occurs rarely (Fig. 50) and in the severe cases it is hardly to be expected.

PLATE 13.

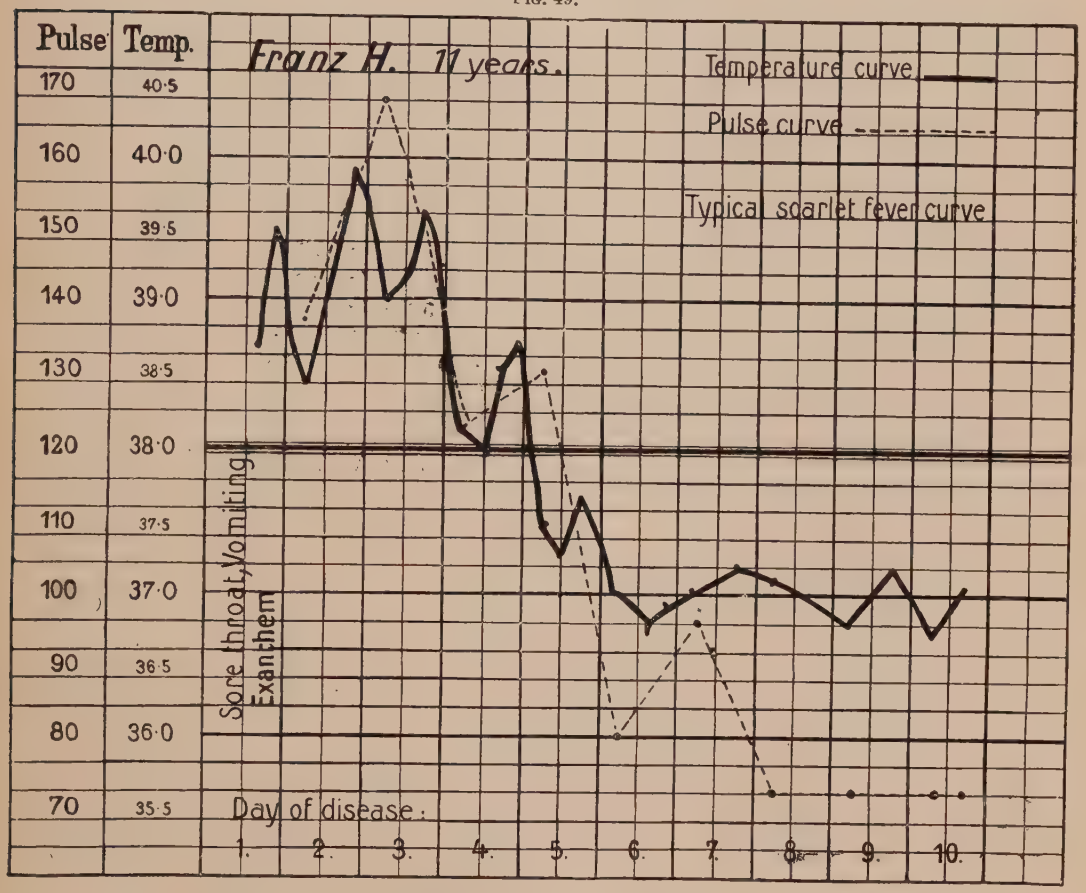


Exanthem of scarlet fever.

a. Eruption on shoulder with miliaria and beginning pigmentation.
b. Eruption fading on upper arm.

In the meantime, changes are taking place in the *skin*. A very fine "dusty" desquamation is seen on the face. At about the middle of the second week desquamation begins on the neck, trunk and inner sides of the thighs, flaky in character, and often in large lamellæ. The palms of the hands and soles of the feet are the last to be involved in this process. Occasionally the entire epidermis is shed, so as to form a veritable cast of the hand and foot (Plate 15). Here, too, desquamation

FIG. 49.



Typical temperature curve in scarlet fever.

may be seen to occur as late as the sixth to eighth week. The nails also present evidences of the disease.

The injury done to the nail-bed at the height of the disease is manifested later by an irregular nail growth. As this portion of the nail is hidden by the nail-wall, the faulty growth is not observed until the nail has pushed it forward into view. This occurs at about the beginning of the sixth week. It is seen best from the seventh to the eighth week, being less marked in young children than in older ones, more so in the severe than in the mild cases, most marked in the thumb-nail. The

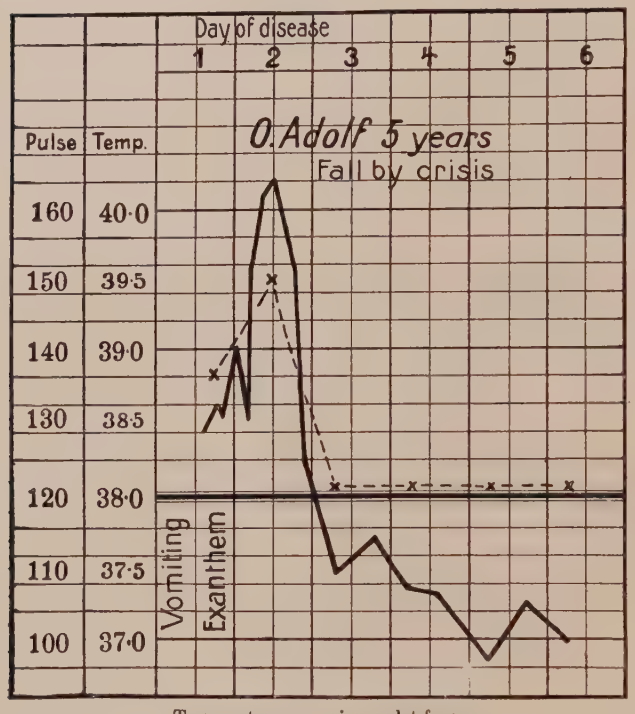
rapidity of the growth of the nail determines the duration of this finding (Heller, Feer). The nail advances 1 mm. in ten days.

The *larynx and lungs* do not participate in the clinical picture in uncomplicated cases. The existence of hoarseness and a laryngeal cough is indicative of a mixed infection, usually the bacillus diphtheriæ. "*Scarlatina evitat laryngem*" was known to the earliest observers.

The *spleen* is at most only slightly swollen; a trifling enlargement of the liver is often to be noted.

So far as the *blood* is concerned, there is present at the height of the disease a high polynuclear leucocytosis. There is also a slight increase of the eosinophiles as well as of the plasma cells, as has been determined by Sluka and myself in as yet unpublished observations. In one fatal case the plasma cells increased to twenty per cent. of the total percentage of leucocytes.

FIG. 50.



Temperature curve in scarlet fever.

Beginning with the fifth day of the disease, the leucocytosis slowly recedes, the normal count being reached early in the third week.

Recent reports indicate that the belief is held by many that the blood serum of scarlet fever patients contains a complement binding substance, and that, therefore, a typical Wassermann's syphilis reaction may be obtained. Insufficient data are as yet on hand to determine the significance of a positive reaction.

In uncomplicated cases of measles, the clinical course is a fairly definite one. This is not true of scarlet fever. The clinical picture is often an exceedingly variable one. In exceptional cases the cardinal symptom of the disease, the eruption, may fail to appear. There is present only the angina (*scarlatina sine exanthemata*). The diagnosis in such cases can be made with certainty only when a typical attack occurs in another member of the family.

Mie G., ten years old, complained of headache in the afternoon, angina in the evening. During the night the temperature rose considerably; no vomiting. The following morning the temperature had receded considerably; the angina had increased in severity. No eruption. Record made on second day of disease. Four days previously a younger sister of the patient had developed a typical case of scarlet fever. When first seen, the skin was pale. Severe redness and swelling of the pharynx; uvula œdematous. Restlessness at night; temperature 39.6° C.; pulse 144. Third day: Skin pale. One lymph-node enlarged to the size of a pea, tender to touch, in the angle of the jaw on both sides. Nose not involved; tongue slightly coated; strawberry appearance absent. Pharyngeal mucous membrane very red, swollen and œdematous; uvula œdematous; small yellowish masses on right tonsil. Fourth day: Uvula, tonsils and edges of anterior faucial pillars blood-red in color; small red spots in surrounding areas, especially in vicinity of uvula. Spots on tonsil larger. No skin eruption. Slight swelling and redness of follicles on skin of trunk.

In the course of the next three days small areas of necrosis appeared on the uvula and the soft palate. Healing of these spots from eighth to eleventh day. Recession of redness of follicles. Fall of temperature by lysis typical. Normal temperature on seventh day. No desquamation.

On the other hand, cases are met with in which the expression of all the symptoms is reduced to a minimum, both in duration and intensity, so that the diagnosis often is not made until characteristic sequelæ appear, or for no apparent reason all the symptoms are suddenly markedly increased in severity, the case terminating fatally inside of twenty-four hours. In such foudroyant cases the characteristic clinical picture is in no wise changed by the rapid course of the disease.

The following cases are illustrative of the two extremes:

Mie W., eight years old; taken to the scarlet fever station on a wrong diagnosis, presented on the morning of the twelfth day, without previous elevation of temperature or vomiting, flushing of the cheeks, a pale red, typical scarlatinal eruption of the trunk, especially on the back, more discrete on the extremities. Right side of pharynx very red. Eruption paled on following day; desquamation of face on sixth day; several days later of trunk.

Henry M., four and a half years old, strong, well-nourished boy. At 7.30 in the morning, vomiting, sore throat, eruption, two thin green stools, followed by lassitude; continued vomiting. At 11 A.M. confluent slightly elevated eruption on trunk, conjunctivitis, tongue heavily coated, redness and swelling of pharynx. Tonsils not coated. Pulse 180, small, irregular. During the afternoon the patient became soporose; extremities, face and mucous membranes cyanotic and cold; deep and frequent respirations (respirations, 54); pulse bad. Death occurred at

9 P.M. Duration of disease, fourteen hours. (At the necropsy, marked status lymphaticus.)

These rapidly fatal cases are exceedingly rare. As a rule, death does not occur, even in the most severe cases, before the third to the fourth day. The symptoms increase in severity progressively. Even in such cases the prodromal symptoms are not of such severity as to excite attention, although the unusually severe course of the disease is apparent. Not until the third or fourth day is the foudroyant nature of the disease fully developed, when the involvement of the nervous system (extreme restlessness, somnolence, anxiety, continuous vomiting) and of the circulation (cold and clammy skin, cyanosis, dark, brownish-red exanthem, bad pulse and dilatation of heart) is the most prominent symptom. The pharynx is red and swollen; the tonsils, if involved at all in the clinical picture, are only coated.

This is a typical so-called *toxic case* of scarlet fever and death occurs as the result of the toxæmia caused by the exciting cause of the disease.

Anatomically, one finds here, first of all, inflammation of the pharynx. Tonsils swollen, soft, containing much exudate, bluish-red in color; gums soft; uvula, posterior portion of tongue and pharynx, dark bluish-red. The hyperæmia is sharply demarcated (Härlin, Heubner).

The *cervical lymph-nodes* are markedly enlarged as the result of an acute, inflammatory infiltration. In fact, the entire lymph system presents evidences of more or less involvement. The solitary lymph follicle and Peyer's patches and other lymph structures in the intestine are swollen; the mesenteric lymph-nodes are hyperæmic, swollen and œdematous.

Changes in the *thyroid* of extreme degree have also been noted (Roger at Garnier, de Quervain, Sarbach). They consist of hyperæmia, desquamation of the alveolar epithelium, decrease in the amount of colloid, with increased fluidity. The interstitial connective tissue remains unchanged. Clinically, there does not appear to be any reason for these conditions.

So far as the *skin* is concerned, the eruption is not visible after death. Schamberg, in his histologic studies of the skin, was able to determine evidences of inflammatory disturbances. Rach confirmed these findings. The most extensive and intense changes occur in the connective tissue surrounding the hair follicles. There is more or less serous and cellular infiltration. Huebler described inflammatory changes in the tissues surrounding the blood vessels. The œdema and pigmentation of the skin, the swelling of the follicles and the sudamina can not be accepted as a reason for the appearance of the eruption. Some observers (Lewkowicz, Poln. Pädiatrie, I, p. 1) are of the opinion that the urticaria is the result of a secondary infection.

In sharp contrast to the toxic form of scarlet fever stands the so-called *infectious form,* in which, in addition to the primary pharyngeal disturbances, there appears on the third to the fifth day of the disease necrosis of the mucous membrane, varying in degree and extent. In these cases the infection extends to the pharynx from the nose and its accessory sinuses (such as the antrum of Highmore), involving later the middle ear, the cervical lymph-nodes, and the lymph-nodes of the lower jaw.

So far as the *pharynx* and regional lymph-nodes are concerned, the changes noted here are present in all fully developed cases of scarlet

FIG. 51.

Posterior pharyngeal wall. Posterior palatine arch. Membrane.

a, membrane and inflammation, ninth day of disease. *b,* eleventh day—inflammation less intense. *c,* thirteenth day. *d,* seventeenth day—small patch of membrane.

fever. They do not in any way invalidate a favorable prognosis, nor do they delay crisis. However, they are apt to be more superficial and reach an early resolution.

In the more severe cases the areas of necrosis appear not only on the surface, but also in the deeper layers of the mucous membrane and often extend as far as the submucosa.

Clinically, the occurrence of these changes is noted, first, in the temperature curve. Instead of the usual morning remission of one or

FIG. 52.

a, membrane on tonsils, uvula and anterior palatine arch, eighth day of disease. *b,* eleventh day—fresh membrane on right palatine arch. *c,* eighteenth day—membrane opposite opening in anterior palatine arch, through which the posterior pharyngeal wall can be seen. *d,* twenty-fifth day—hole larger, marked deformity of anterior palatine arch, uvula drawn to left side.

more degrees, noted on the third or fourth day, the temperature falls only a fraction of a degree and the afternoon temperature, which ordinarily exhibits a steady fall, is now seen to rise. Consequently, the characteristic lysis does not appear.

On inspection, the *pharynx* is seen to be considerably more swollen, the necrotic spots are covered with a dirty gray exudate, which rapidly changes in color to a dirty yellowish-white, resembling the exudate of

diphtheria. Microscopically, it is found to contain but little fibrin and many micro-organisms, especially streptococci. Only in exceptional cases is this coating distinctly membranous in character, as in diphtheria, and then it contains considerable fibrin in addition to the streptococci. Inasmuch as the necrosis mentioned above does not confine itself to the pharynx and tonsils, but may extend to the uvula and soft palate, it is not always possible to exclude a diphtheritic infection. In doubtful cases a bacteriologic examination alone can determine the nature of the infection.

In the *favorably progressing cases* there is little or no involvement of the nose, and the ulcers heal. The necrosis of the mucous membrane is apparent only in the anterior faucial pillars. They stand out prominently and their edges are ragged (Figs. 51 and 52). The tonsils appear to have lost some of their substance; their surfaces are nodular. The temperature falls by lysis unless further complications (ear, lymph-nodes) make their appearance.

In the more *severe cases* the pathologic picture increases in severity. The ulcers on the soft palate extend further into the tissues, and there may be considerable destruction of the soft palate as well as of the uvula. In some cases the necrosis in the tonsils extends to the anterior faucial pillars and may progress to perforation. This may be so extensive as to cause a collapse of the soft palate. A perforation at the base of the uvula may also occur, as the result of extension from the pharyngeal tonsil.

In these cases the process is not limited to the pharynx. Analogous changes are found in the nose and, in the most severe cases, in the larynx.

In those cases where the swelling of the mucous membrane of the pharynx and nose is slight, there is comparatively little interference with inspiration. However, as the changes in the nose become more intense, nasal respiration is impeded and sometimes impossible. The secretion from the nose is profuse, purulent, and malodorous. The skin of the nostrils is irritated. Mouth-breathing alone gives relief; the lips, mouth and tongue are dry, the tongue is leathery and coated, the lips are cracked and there may be necrosis of the buccal mucosa. The accessory sinuses of the nose are similarly involved (antrum of Highmore, sinus frontalis). Because of the disturbed respiration, the patient is restless and sleeps badly.

Involvement of the middle ear is almost a certainty. The inflammatory changes lead rapidly to spontaneous perforation of the tympanum and to an otorrhœa, slight in degree, but of considerable duration.

As a rule, the sudden onset of pain in the ear and the pressure tenderness around the ear is sufficient evidence of an impending otitis,

but in all cases, even when these warning symptoms are not present, it is advisable to examine the ear with the mirror, because the otitis may otherwise often be overlooked.

The ear complications in scarlet fever are of considerable prognostic significance. They often result in a permanent impairment of hearing. Statistics show that scarlet fever is one of the most frequent causes of auditory disturbances.

The condition of the patient is a most uncomfortable one. The temperature remains elevated so long as the disturbances in the mouth and throat are active; there is considerable loss of appetite; the ingestion of food is difficult. Therefore, the patient is made to suffer from the local process, which causes the toxæmia, and the weakness which results from the insufficient amount of food ingested.

It has as yet not been determined whether the systemic infection is the result of the entrance of streptococci into the general circulation, or merely the result of the absorption of their toxins. In most cases it is probably a streptococcæmia and not a toxæmia. The death of the tissue probably is caused by the as yet unknown bacterial cause of scarlet fever. The streptococci would in all probability not make their way into the tissues until after necrosis has occurred.

The changes in the lymph-nodes are deserving of special mention at this time. In every case of scarlet fever there is some swelling of the lymph-nodes at the angle of the jaw.

Enlargement of the lymph-nodes elsewhere is as observed in the living only in cases of extrabuccal infection. Such patients as come to the necropsy are found to have swelling of the lymph-nodes in other regions, notably in the deep cervical lymph chains, the mesenteric lymph-nodes and the lymph structures of the intestines.

The degree of enlargement of the lymph-nodes at the angle of the jaw is in no wise dependent on the severity of the pharyngeal inflammation. The moderate involvement seen in uncomplicated cases of scarlet fever recedes concomitantly with the other symptoms. Sometimes the nodes do not regain their normal size; they remain permanently enlarged, occasionally becoming even larger or undergoing suppuration. In such cases a smooth convalescence is denied the patient and recovery is protracted.

The lymph-node enlargement which accompanies the severe grades of scarlet fever may recede to normal, without suppuration. On the other hand, in the worst cases of the infectious type of the disease, the lymph-node involvement may assume alarming proportions. Not only are the nodes themselves involved, but the surrounding tissues are infiltrated and œdematous, thus forming a dense mass without circumscribed pus formation.

Areas of hæmorrhagic inflammation are seen, as in plague (plague-like form of scarlet fever).

The œdema may extend as far as the sternum. Pressure on the trachea may cause dyspnœa. In the case of a child, two and a half years old, we were obliged to do a tracheotomy on the twenty-seventh day. Death ensued shortly afterward, however. Incision of the mass did not give the patient any relief. There was no pus.

When suppuration of these masses does occur, it may extend to the neighboring tissues (vessels, mediastinum).

The prognosis in the severe anginose cases is always grave. At best, resolution is delayed until the third week. Perforations of the anterior pillars may heal. Plate 14, *b*, represents such a case, but, as a rule, the prognosis in such cases is bad. In the more rapidly progressing cases death results at the end of the first or the beginning of the second week. Occasionally it does not occur until the third or even the fifth week. The longer a fatal termination is deferred, the more varied are the complications.

The condition may progress to gangrene. In the case of a child, aged three and three-quarter years, brought to the hospital in a moribund condition, in the fifth week of the disease, the gangrene had involved the œsophagus as far as the cardia. Isolated patches of mucous membrane were found in the vicinity of the bifurcation.

Entrance of the streptococci into the general circulation may lead to secondary infections in the pericardium and peritoneum; more rarely a general pyæmia results, with the formation of metastatic abscesses in other organs as well as in points. Then, again, death may ensue from a lobular pneumonia, which progresses to suppuration and pleurisy. In these cases the clinical picture of scarlatina is completely overshadowed by the septic complications.

Another complication to be dreaded is the extension of the otitis to the *mastoid* and from here to the meninges. Marked tenderness on pressure over the mastoid region is the first symptom to direct attention to such extension. The overlying skin is red and swollen. Increase in the degree of swelling causes crowding away of the ear.

Olga Schw., two and a half years old. Severe case of scarlet fever; infectious manifestations on sixth day. Left tympanum slightly reddened on seventh day; otorrhœa on ninth day. Right tympanum reddened on tenth day; otorrhœa on fourteenth day; bilateral. Fifteenth day: Skin behind right ear reddened; ear protruding. Sixteenth day: Incision of subperiosteal abscess. Seventeenth day: Complete right facial paralysis. Restlessness increased in the course of the next few days; condition of patient becoming progressively worse. Twenty-first day: Tremor of hands; gnashing of teeth; unconsciousness at noon;

PLATE 14.

a. Gangrene after scarlet fever in a syphilitic child.
b. Enanthem on the intestinal mucosa with follicular hæmorrhages in septic scarlet fever.

general convulsions, beginning in the left upper extremity. Death. Necropsy showed purulent meningitis. Microscopically, the exudate was seen to contain streptococci and a Gram positive bacillus, resembling the bacillus influenzæ.

A radical operation on the mastoid will often prove effective in preventing extension of the inflammation to the meninges. A brain abscess may develop and, if possible, surgical intervention should be resorted to at once in such cases.

I saw a three-year-old child die eighteen months after the commencement of a scarlet fever otitis, which had resulted in a brain abscess without any clinical manifestations.

It must be borne in mind that in the case of a so-called extrabuccal scarlatina the necrotic inflammation, which ordinarily is seen in the pharynx, may reach its development at the infection atrium. The surgical wound, or other injury—in puerperal scarlatina, the trauma of the genitals—has the appearance of an infected wound. Its edges are infiltrated, the secretion covering the wound resembling macroscopically and microscopically the condition ordinarily seen in the pharynx, necrotic masses of connective tissue are seen in the depth of the wound, and the regional lymph-nodes are enlarged. Streptococci are always found in the wound secretions.

If the infection extends from one or more papules, marked inflammatory changes are here also evident. In cases of extrabuccal scarlet fever the skin eruption is, as a rule, most intense in the vicinity of the infection atrium. The mucous membrane of the mouth and pharynx does not show the usual eruption; it is merely reddened and swollen.

OTHER COMPLICATIONS OF PRIMARY SCARLET FEVER

A comparatively harmless complication of primary scarlet fever localizes itself in the *joints*. In from five to eight per cent. of all cases it makes its appearance at the end of the first or the beginning of the second week.

Such an extension manifests itself rather suddenly as a symmetrical painful swelling, usually of the hand, finger, ankle- and knee-joints. Other joints are involved but seldom. Older children complain of pain in the affected joints; in the case of younger children attention is directed to this complication by the absence of motion in the affected joints.

The joints the seat of such inflammation are hot to the touch, there is some œdema, the skin over the swelling is diffusely or sometimes discretely reddened. Suppuration fortunately never occurs. The inflammation persists for from three to seven days, seldom longer, and is almost without exception accompanied by fever. The characteristic lysis occurring at the end of the first week of scarlet fever is delayed.

For two or three days there is a step-like rise in the temperature and then the temperature falls to normal by lysis.

The etiology of *scarlatinal synovitis* is as yet little understood. It is uncertain whether it is of toxic or infectious origin. It must not be confused with the arthritis of pyæmic origin mentioned above.

In some cases there is pain only, no swelling, in the affected joints.

Josef, aged seven years. Light attack of scarlet fever. Temperature falls by lysis from 39° C. on the third day (afternoon) to 37.5° C. on the morning of the sixth day. On the seventh day lysis is interrupted; step-like rise in temperature, reaching 39.3° on the ninth day. From then on lysis.

Eighth day: Pain in both wrist-joints, without swelling.

Ninth to eleventh day: Pain continuous.

Twelfth day: Pain in the wrist-joints less severe; slight pain in ankle-joints.

Thirteenth day: Pain disappeared.

The *heart* shows evidences of involvement early in the disease. The first sign is the increased frequency of the pulse rate. This frequency, as was shown by Trousseau, is out of all proportion to the elevation of the temperature and the age of the patient. A pulse-beat of 150 to 160 in four-year-olds, 120 to 140 in older children (seven to twelve years), is common with a temperature of 39° to 40° C. (102° to 104° F.). This occurrence is not of prognostic significance.

Widening of the cardiac area of dulness transversely is sometimes noted during the first few days of the disease in severe cases; greater dilatation occurs usually only in foudroyant cases. Anatomically, there are noted, in addition to degenerative processes, genuine myocardial changes (Romberg). The weakened heart action is made evident by the lowered pulse tension, but more particularly by the fact that in spite of the high internal temperature, a cool sponge bath will immediately lower the temperature and cause cyanosis of the peripheral parts. As the result of the weak heart action and the disturbed circulation, the eruption takes on a dirty, dark-red, even bluish-red color, the skin in the most severe cases becoming deathly pale in color, and on finger pressure the area of anæmia changes to hyperæmic very slowly. Finally, the eruption may give way to a general cyanosis. As everyone knows, it is in cases such as these that it is stated that the eruption "was driven inward." This change in color of the eruption, the result of a circulatory disturbance, is of prognostic significance.

Pospischill recently called attention to the fact that in many cases of scarlet fever a characteristic early symptom is a scratching sound (pericardial in tone), heard at the base. Berkholz confirmed this statement. Other systolic sounds are often heard at the height of the disease,

and even later in many cases. They are basal in character, the point of maximum intensity being over the pulmonary area. They are not of prognostic significance. It is rather difficult to state why they occur.

Important, although by no means frequent, are the changes in the structure of the heart valves. Next to rheumatism, scarlet fever is the most common cause for the development of valvular defects. There does not appear to be any definite relationship between the scarlatinous synovitis and the endocarditis.

That both complications may occur in the same patient is seen in the following case, that of an eleven-year-old girl, who suffered from a mild attack of the disease (maximum temperature, 39.2° C., 102.5° F., on the second day). Lysis was interrupted on the sixth day by the occurrence of a synovitis in both wrists (swelling of the right wrist). On the eighth day the swelling diminished in extent; on the ninth day the temperature fell to 38° C. (100° F.), but not until the fifteenth day was the normal temperature reached. The heart was normal until the twelfth day, when the apex beat passed from the fourth intercostal space, inside of the mammillary line to 1 cm. to the left of the mammillary line. Heart action became more rapid, of pendulum-like rhythm.

On the fourteenth day, increased heart action, soft systolic and short diastolic sounds at the apex. Both sounds, as well as increased area of cardiac dulness, present until the dismissal of the patient on the thirty-second day. According to the mother of the patient, the child has remained perfectly well since.

It is not often possible to determine the exact time when the endocarditis first appears. As a rule, the onset of this complication is extremely insidious, without any subjective manifestations. Eternal vigilance is necessary if one wishes to learn of the existence of the endocarditis at the earliest possible moment. Otherwise, its presence may go unnoticed.

Also of great importance are those cardiac complications which make their appearance in about five per cent. of the cases at the end of the first or the beginning of the second week, seldom later than this (fifth week).

Anna P., ten years old, entered hospital on first day of disease. Mild attack of scarlet fever (maximum temperature, 39.3° C. on third day). No evidence of circulatory disturbance other than the typical primary increased frequency of pulse rate. Decline of temperature by lysis, beginning on third day; uninterrupted decline.

In spite of this apparently smooth progress of the disease, the cardiac disturbance is none the less severe, the first symptom being noted on the sixth day, at a time when all the active manifestations of the disease are receding. The first heart tone becomes impaired. The following

day the pulse and heart action are lessened in frequency (pulse, 80) and become arrhythmic; on the eighth day cardiac dulness extends to the left, the apex beat is heaving and more visible. At the same time the first tone is displaced by a distinctly systolic murmur. In the evening the patient complains of palpitation. The arrhythmia, bradycardia, dilatation and systolic murmur continue unchanged till the end of the third week. No subjective symptoms are noted. On the twenty-third day no symptoms are evident.

In some cases the symptomatology of cardiac disturbances is more complicated, because the condition becomes worse. The second pulmonic sound is accentuated; there is duplication of the second tone at the apex, less often of the first. The pulse is small and weak; the afternoon temperature may rise to 38° C. (100.4° F.), but not higher. Some children become strikingly pale; the face is puffy. There is usually more or less feeling of lassitude and weariness. In marked contrast to the post-diphtheritic cardiac disturbances, of which the condition strongly reminds one, the majority of these children feel entirely well. The clinical picture of these cases is never so severe as is seen in diphtheria. Sudden death never occurs. The fact that these cardiac disturbances are met with almost exclusively in the mild cases of scarlet fever may be accepted as evidence that they are caused by the products of the infection, *i.e.*, a toxæmia. But it is impossible to determine whether a myocarditis is the basis of this disturbance. I have proposed the name *myasthenia cordis* for this affection. In almost fifty per cent. of these cases resolution occurs in from two to three weeks; in the remaining fifty per cent. there is a permanent systolic murmur, arrhythmia and enlargement of the heart, although the patient is not invalided in the least.

I have previously emphasized the fact that variations in the temperature curve accompany the occurrence of all complications in primary cases of scarlet fever. It is by no means uncommon to have a continued elevation of temperature even when there has been complete recession of all symptoms. And no explanation can be found for this. Often lysis does not occur in these cases until the end of the third week. It is customary to designate this a secondary fever (Fürbringer), and to assume that it is caused by some local infection which has either escaped or defied detection. Careful and thorough investigation of these cases will diminish their number considerably. Special attention should be paid to the pharynx, nose, middle ear, and the lymph-nodes.

A comparatively rare complication of primary scarlet fever is *pneumonia*.

If this complication sets in at the height of the disease—and here usually only small children are concerned—the prognosis becomes considerably more grave, because almost invariably it leads to infection of

the pleura, which, in turn, is followed by an empyema, very often fatal, with a thin fluid pus containing streptococci.

In the case of a child, twenty-two months old (the pneumonia appearing on the first day, and death occurring on the fourth day), there was a hæmorrhagic pneumonia, septic in character, in the left lower lobe (streptococci in exudate), and a pleurisy in the vicinity of the part of lung affected.

In the case of a boy, two and a half years old (pneumonia beginning on second day, empyema on the fifth and death occurring on the ninth day), there appeared symptoms indicative of a pneumonic involvement of the lower half of the left upper lobe, with central necrosis.

In both cases the pharyngeal picture remained unchanged, so that one might have believed that the lung was the infection atrium.

Other complications referable to the respiratory tract are usually the result of a mixed infection, most often *influenza*. I recall very distinctly that among ten children lodged on one floor of the scarlet fever pavilion, four (five to eight years old) suffered from a complicating influenzal pneumonia, fortunately terminating in recovery.

DIFFERENTIAL DIAGNOSIS

The recognition of a typical case of scarlet fever is by no means difficult. The acute onset of the initial symptoms, the early marked involvement of the gastro-intestinal tract, the prominence of the pharyngeal symptoms, the macular character of the exanthem, the slight increase in size of the individual macules, their bright red color, and the circumoral triangular area of paleness will easily distinguish this condition from measles. The diagnosis of *measles* is based on the catarrhal symptoms (sneezing, coughing, conjunctivitis) appearing several days before the eruption, Koplik's spots on the buccal mucous membrane, the location of the eruption within the circumoral triangular area of paleness of scarlet fever, the larger size of the macules and their greater prominence. At first they are small, but rapidly increase in size. They show considerably more variation in size than do the spots in scarlet fever.

After the subsidence of the acute symptoms there is seen a rather intense spotted pigmentation of the skin, which persists for a longer time than in the case of scarlet fever. The trail of the scarlet fever consists in a rather severe redness of the pharynx, angina and raspberry tongue. To base a diagnosis on the character of the desquamation necessitates considerable caution. Only large scales speak with certainty for scarlet fever.

It is not infrequent, however, that the eruptions of scarlet fever and measles are atypical. I have called attention to the occurrence of a morbillous efflorescence (double eruption) in severe cases of scarlet fever. The diagnosis is still further obscured by the appearance in such

cases of coryza and conjunctivitis. Furthermore, I have frequently observed that after the fastigium of measles has been passed, the eruption, especially on the extremities, assumes the macular character seen in scarlet fever, and which is so characteristic of that disease. Therefore, it behooves the observer to proceed cautiously in arriving at a diagnosis, particularly when at various points examples of both types of eruption stand side by side.

The eruption of *rötheln*, or German measles, consists of considerably smaller macules than in the case of measles, so that it more nearly resembles the eruption of scarlet fever; however, the arrangement of the eruption on the face is similar to that seen in measles. The distance between the macules on the trunk and extremities in rötheln is greater than in the case of scarlet fever. Swelling of the lymph-nodes of the nape of the neck supports the diagnosis of rötheln.

The eruption in *erythema infectiosum* on the face is like that of scarlet fever; on the extremities the individual spots are large and are most intense in their coloring on the extensor surfaces.

The greatest difficulty in diagnosis, as in the case of all eruptive diseases, is met with in those mild cases in which the symptoms are illy defined. So far as the eruption itself is concerned, confusion is apt to result when there is redness of the skin accompanying any febrile condition. The circumoral triangular area of anæmia may be present, but on the skin of the extremities the eruption is more diffuse, without any macules; there is no œdema of the skin or pigmentation of the icteric type. It is merely a case of *hyperæmia of the skin.*

The *exanthem seen in crying infants* bears a very close resemblance to the eruption of scarlet fever, but is easily differentiated from the latter in that it disappears quickly with the cessation of the crying. The reddening of the skin, known as blushing, also comes in this class.

It is by no means easy to differentiate the *eczema and sudamina* seen in small children, especially during the early years of life. Of course, a valuable point in diagnosis is the fact that children are rarely affected with scarlet fever during the first year of life. However, all these things merely emphasize the fact that a diagnosis of scarlet fever is never to be based on the appearance of the skin. I have seen sixteen cases of scarlet fever in children under one year of age; the youngest child was four months old. Three children were less than six months old.

The reddening of the skin consequent on local application (water, oil) is always limited in extent, confined to the area of application.

Drug eruptions (atropin, aspirin, iodoform, chrysarobin, tuberculin) have also been known to simulate the scarlet fever eruption. A knowledge of the use of any of these drugs and the appearance of the fauces will aid in arriving at a correct diagnosis. The tuberculin eruption is

purely follicular in character; the individual follicles are red and swollen. The greatest difficulty in diagnosis is presented by the scarlatiniform eruption of *serum disease*, and the appearance of the pharynx and fauces in a case of diphtheria in recession is such as to make a correct diagnosis almost impossible. Many observers have pronounced every scarlatiniform eruption consequent on the injection of serum or antitoxin as indicative of scarlet fever. That is surely going too far in our diagnosis. Only an intense eruption and a severe angina are diagnostic of scarlet fever. The eruption of serum disease is pink in color and extends from the site of the injection.

The variations in intensity of the pharyngeal inflammation of scarlet fever from a simple redness and swelling to an extensive necrosis of the so-called diphtheritic membrane lead to errors in diagnosis very frequently, and call for considerable diagnostic acumen, particularly in view of the fact that the anginose inflammation of scarlet fever is present before there is any evidence of a skin eruption. In such cases it may be necessary to postpone a diagnosis for twenty-four or even forty-eight hours. However, vomiting, with severe reddening and swelling of the fauces, should always direct attention to the possibility of the case being one of scarlet fever.

Pathognomonic of *diphtheria* are a spreading of the membrane on the first or second day of the disease to other parts of the pharynx and fauces, the characteristic elastic appearance of the membrane, and its appearance on the uvula, anterior pillars of the fauces and posterior wall of the pharynx. If an eruption also makes its appearance, it is an evidence of mixed infection. In such cases a positive diagnosis must be based on a bacteriologic examination.

As the disease progresses, the nature, extent and localization of the throat membrane are of considerably less value in arriving at a diagnosis of scarlet fever. The slimy character of the membrane, the destruction of the deeper layers of the mucous membrane and the raspberry tongue are pathognomonic of scarlet fever rather than of diphtheria. Microscopic examination of a smear preparation will show an abundance of streptococci. This tendency to necrosis is seen only in syphilis, tuberculosis and scarlet fever.

I saw such a necrosis of the pharyngeal mucous membrane in two sisters, the victims of tuberculosis. Instead of the hyperæmia seen in scarlet fever, there was a marked anæmia of the mucous membrane, and a chronic, painless swelling of the cervical lymph-nodes. Finding the tubercle bacillus in the smear preparation increased the difficulty of arriving at a correct diagnosis. Both children also had an advanced tuberculosis of the lungs, which shortly led to a fatal termination in both cases.

PROGNOSIS

To make a correct prognosis in scarlet fever is a matter of no small moment. Even when the onset of the disease is exceedingly mild in character, tempting one to pronounce the case a mild one, all the symptoms may rapidly increase in severity, so that it is impossible to make a correct prognosis on the first or second day of the disease. On the third or fourth day, when the progress of the pharyngeal inflammation may be determined with some degree of certainty, the prognosis must be restricted to the primary disease. It is impossible to foresee the occurrence of complications.

From the diagnostic standpoint, Moser divided scarlet fever cases into favorable (1 and 2), doubtful (3), and lethal (4) cases. Prognosis 1 included those cases which did not present any severe symptoms, in which there was a low temperature, slight or no pharyngeal involvement, typical eruption and no constitutional symptoms. Prognosis 2 included those cases in which certain symptoms were predominant, being more severe than others, without apparently being inimical to life, such as a moderate degree of pharyngeal involvement, the nose not being affected, intense eruption, with no evidence of cardiac weakness (absence of cyanosis, cold and clammy skin, pulse of good quality), high temperature.

Prognosis 3 and 4 included the severe cases, those cases in which either the toxic or infectious symptoms predominate, although they are often seen in combination. The age of the patient also enters into consideration as a factor in the prognosis. Children between the ages of one and four years are in greater danger than older children.

The severe purely toxic cases are characterized by an intense eruption, with eventual occurrence of the double eruption, and conjunctivitis. Symptoms of cardiac weakness are always present (cyanosis, cold and clammy extremities, dark red, dirty or bluish-red color of the eruption, and in the most severe cases the eruption is obscured by a general cyanosis). The face is sunken. Sensory symptoms are marked. Restlessness, jactitation, convulsions, toxic frequent and deep respiration are of graver prognostic significance than a mere lethargy or delirium. Persistent vomiting and green, liquid, malodorous stools complete the clinical picture of these severe cases of scarlet fever.

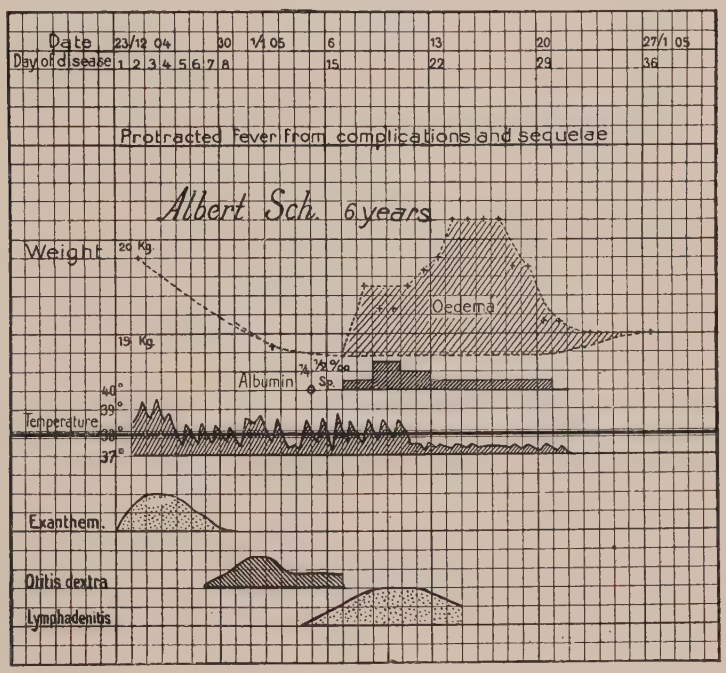
The onset of infectious symptoms (coryza, pharyngeal necrosis, otitis and greater involvement of the lymph-nodes) obscures the prognosis, because defervescence is postponed. So far as a fatal termination is concerned, the prognosis depends entirely on the extension and severity of the nasal and pharyngeal involvement and the intensity of the lymphadenitis. An unfavorable prognosis may be made early in

such cases in which there appears soon after the onset of the disease an intense swelling of the upper cervical region.

Gangrene of the pharyngeal mucous membrane and the appearance of a pyæmia invariably lead to a fatal termination, and, therefore, in such cases, Prognosis 4 is justified.

I wish, again, to call attention to the significance of the temperature curve in scarlet fever. The height to which the temperature may go is not of prognostic significance, but it is of the greatest importance to observe closely the temperature curve. A study of this curve, as in the

FIG. 53.



Continued fever in scarlet fever.

case of typhoid, will be of considerable assistance in making a prognosis. The appearance of each and every complication or increase in severity of the symptoms is quickly made manifest in a rise in the temperature. Often a slight variation in the temperature curve will direct attention to the onset of a complication; in fact, this may be the first symptom, subjective or objective.

SEQUELÆ OF SCARLET FEVER

Unfortunately, the danger point in scarlet fever is not passed with the subsidence of the primary disease and its complications. There is now initiated the period of the sequelæ, which may defer complete convalescence for weeks, and which, in some cases, may lead to death. In the severe cases, where the patient survives the fourth week of the

disease, dangerous and fatal sequelæ may complete the clinical picture of the case. It is a notable fact, however, that the mild cases of scarlet fever are most often followed by sequelæ.

The time of appearance or onset of the sequelæ is characteristic. There is more or less uniformity in this regard. They may appear as early as the twelfth day, but not later than the sixth week after the subsidence of the primary disease. They appear most frequently during the third week (critical days are the nineteenth to the twenty-first).

At the Vienna Clinic, in 1904 and 1905, post-scarlatinous lymphadenitis and nephritis occurred as follows (counting from the beginning of the scarlet fever):

Week.	Lymphadenitis.	Nephritis.
2 (12th to 14th day)	2	2
3	37	18
4	22	7
5	6	3
6	1	3

After the fourth week the frequency of the appearance of sequelæ diminishes rapidly. It is not until the seventh week, however, that one may assume with certainty that no sequelæ will manifest themselves. The latest time of onset of a lymphadenitis was the forty-first day of the disease.

A second characteristic of the onset of sequelæ is the acuteness of the symptoms, the remittent type of the fever, and, as in the primary affection, its tendency to fall by lysis.

Oscar B., aged eight years (Fig. 54). Eruption slight in degree. Lacunar angina; maximum temperature, 39.2° C. (102.5° F.); desquamation. Normal temperature from the fifth to the seventeenth day. On the afternoon of the seventeenth day, 38° C. (100° F.), on the next day, 38.8° C. (101° F.). In the angle of the jaw on the right side, a bean-sized lymph-node, tender to touch. No albumin in urine (nor at any subsequent time). Nineteenth day: Maximum temperature, 39.2° C. (102.5° F.). Lymph-node somewhat larger; in the afternoon, pain in the left ankle-joint, with swelling and redness of the skin in spots. Twenty-first day: Swelling of lymph-nodes lessening. Ankle-joint unchanged. Pain and fever subside on the twenty-second day, and the swelling on the twenty-third.

In this case the affection of the lymph-node was accompanied with a joint involvement. It is apparent, then, that various sequelæ may appear, either singly or in combination. Children in the same family may manifest the same temperature curve and still be suffering from different sequelæ. The sequelæ which may make their appearance are, first, nephritis, and, second, conditions whose relationship to the nephritis was at one time not appreciated: Lymphadenitis, synovitis, endocarditis, simple fever without apparent cause, and recurrent attack of scarlet fever.

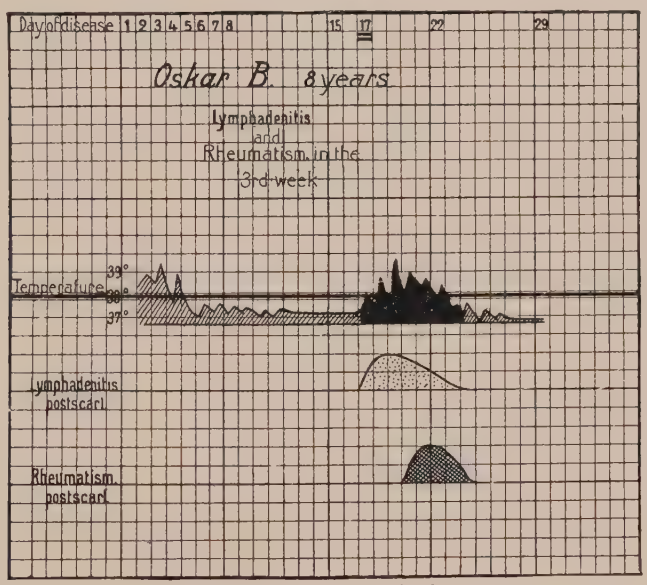
NEPHRITIS

The nephritis is usually ushered in with vomiting, loss of appetite and rise in temperature. The face is pale, and sometimes the first symptom manifested is a characteristic puffiness of the eyelids.

So far as the kidney itself is concerned, there is at first found a trace of albumin in the urine; in the course of two or three days the urine contains blood and is rich in sediment. Then, again, the nephritis is ushered in with hæmaturia, as in the following case, when other severe initial symptoms (lymphadenitis, high fever) direct attention to the condition.

Herminie M., aged four years. Moderately severe attack of scarlet fever, with fever until the sixteenth day caused by a complicating syno-

FIG. 54.



Temperature curve in scarlet fever.

vitis and otitis. On the twentieth and twenty-first days, fresh joint pains; then no temperature elevation until the thirtieth day. At four o'clock in the afternoon, 37.1° C. (98.6° F.); patient cheerful. At six o'clock, the patient complains of pain in the region of the angle of the jaw on the right side; inside of four hours the temperature rises to 40.9° C. (105.8° F.); pulse, 200. The following morning, temperature, 38.4° C. (101° F.); at the angle of the jaw on the right side, a painful lymph-node, size of a bean, surrounded by a diffuse swelling.

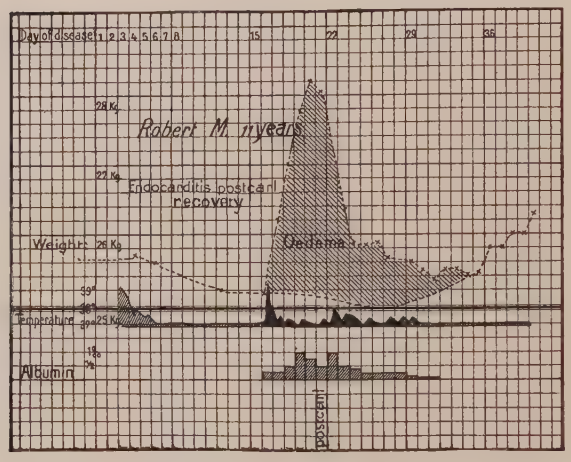
In the morning of the thirty-second day, temperature, 37.8° C. (99° F.); morning urine free of albumin; temperature at noon, 40.4° C. (104° F.). At 2 P.M., sudden hæmaturia (not much blood). Frequent vomiting; appearance of a fleeting eruption, consisting of large macules. Urine contains much sediment. Intermitting temperature of high

degree continues until the thirty-fifth day. Blood disappears from the urine on the thirty-seventh day; albumin disappears on the forty-sixth day (maximum amount of albumin on the thirty-third day, ½ per cent.). Complete recovery.

In cases where the hæmaturia is the initial symptom, it is so evident that it is hardly possible to overlook the kidney complication. Even in the case of small children, who are apt to void the urine on the bedding, the presence of blood is shown by the brownish spots on the bed linen.

The urine may be cloudy, bright red, brownish-red and deposits a considerable sediment. The brownish-red color does not by any means indicate a nephritis of severe grade; in fact, the urine may be of this color from the beginning of the trouble. The sediment consists of all kinds of casts, fresh and disintegrated red corpuscles.

Fig. 55.



Temperature curve in scarlet fever.

Chemically, the urine contains albumin in quantities of from one-quarter to ten per cent., seldom more than this. It is important to examine the urine (heat, acetic acid and potassium ferrocyanide tests), because often traces of albumin appear in the urine just before the onset of the hæmaturia, and, in some instances, the albuminuria is the only symptom in mild grades of nephritis.

Another symptom is a diminished quantity of urine. Unless there is also a hæmaturia, this diminution is apparent only when it is extreme. Whenever traces of albumin are detected, the twenty-four-hour specimen should be collected and the amount carefully measured. From the prognostic standpoint, this is of the greatest importance.

Of equal significance is the daily record of the body weight, although in private practice this is not often possible. Variations in body weight are indicative of a rise and fall in the grade of œdema, which so often is a symptom in nephritis. This is likewise of prognostic value.

Unlike the œdema occurring in cases of heart disease, the œdema of nephritis may be seen not only in the dependent portions of the body (hypostatic œdema), but especially in the face (eyelids), the feet and in the scrotum. In severe grades of œdema, fluid gathers in the serous

cavities (ascites and hydrothorax), and a general anasarca may result. The appearance and disappearance of the œdema often succeed rapidly on one another, as in the following typical case of a well-developed nephritis:

Robert M., aged eleven years (Fig. 55). On the third day presented an intense scarlatinal eruption, but only a slight pharyngeal inflammation. Inside of two days temperature fell to normal. Desquamation; general condition good until the sixteenth day.

Sixteenth day: Traces of albumin in the morning urine; at noon temperature rose to 39.2°; vomiting at one o'clock, followed by continued retching. General weakness; face puffy.

Seventeenth day: Increase in body weight of one kg. Twenty-four hours urine only half the normal amount (about 400 c.c.); contains one-quarter per cent. albumin; no sediment. Heart action slow (bradycardia).

Eighteenth day: Urinary sediment contains many granular and a few hyaline casts. Pulse, 72 (had been wavering between 90 and 120).

Twentieth day: Maximum body weight, 3 kg.; œdema; urine reddish in color; much sediment containing epithelial and granular casts, a considerable number of red blood corpuscles, blood platelets, and ¾ per cent. albumin. Pulse in the morning, 96; headache and lassitude during the day. At 12.30 A.M., muscular twitching, beginning in the face muscles, extending quickly over the entire body, most pronounced on the right side. Loss of consciousness, face pale, lips cyanotic, foaming at the mouth. Pulse, 150. Continuous convulsions at midnight. Venesection, removing about 200 c.c. of blood through the right median vein. Infusion of 200 c.c. physiologic saline solution into skin of abdomen. Convulsions less frequent and at longer intervals. Slight twitching until 4 A.M.

Twenty-first day: Weakness, sensorium unimpaired. Occasional twitchings of slight degree; retching. Fifteen to twenty green, fluid stools, containing mucus. Drank during day ¼ liter Biliner water. Urine, about 250 c.c.; bloody. Sediment as before.

Twenty-third day: Body weight, 1.7 kg. less. Continued diarrhœa. Urine scanty; very bloody.

On the twenty-fourth day urine increased in amount (without medication other than venesection); 2000 c.c. voided on thirty-second day. No sediment since nineteenth day; no albumin after thirty-second day. Convalescence; great gain in weight. Discharged on forty-ninth day.

The particular danger to be apprehended from a nephritis is the appearance of uræmia, which often, as in this case, occurs suddenly in the course of an apparently mild case. As a rule, however, the uræmic symptoms are preceded for several days by mild disturbances, such as

continuous headache, severe colic, retching, eyes staring, slow pulse of high tension.

An additional danger to be feared in these cases is weak heart action. Irrespective of the anxiety shown by the patient in cases of heart failure, which is more or less of a subjective nature, are the respiratory symptoms, such as frequent superficial respiration, and cyanosis of the mucous membranes. In the most severe cases death occurs with symptoms of pulmonary œdema.

Julius R., three years old. Light attack of scarlet fever. Beginning on the eleventh day the pulse is arrhythmic, slow, 64, in spite of rise in temperature and swelling of the lymph-nodes.

Fourteenth day: Traces of albumin.

Sixteenth day: One per cent. of albumin, bloody urine, increase in body weight.

Eighteenth day: Dyspnœa in the evening. Orthopnœa; blood pressure, 165 mm. (Gärtner).

Twentieth day: Evening temperature, 41° C. (105.5° F.); pulse, 192; increased dyspnœa; cyanosis of mucous membranes; mental faculties unimpaired. Sputum foamy.

Twenty-first day: Temperature 40.6° C. (105° F.). Death in the afternoon, with clonic convulsions.

Dyspnœa is not always a symptom of pulmonary œdema. It may accompany a bilateral hydrothorax, especially when there are present evidences of pleurisy.

Adolf G., five years old. Had scarlet fever three weeks ago. Nephritis, with bloody urine; two per cent. albumin; typical sediment. Dulness over both lungs, especially posteriorly, from the seventh dorsal vertebra on downward. Distinct pleural friction sound above the line of dulness. Cardiac area of dulness increased markedly laterally (to the right sternal border on the right, and on the left to the apex, which is in the mammary line, to the fifth intercostal space outside of the mammary line). No pericardial friction sound. Liver dulness, 4 cm. below the costal border. Pulse small, soft, of poor tension. Dyspnœa and cyanosis. Diagnosis: Nephritis, with secondary inflammatory processes of both pleuræ; hydrothorax; hydropericardium; weak heart. Rapid improvement on the administration of digitalis. Seven days later the heart is normal. Kidney lesion healed after seven weeks.

Although in this case there were present hydropericardium and symptoms of heart failure, the patient recovered. Of far more serious import as a complication of nephritis is pneumonia, which may be an additional cause of dyspnœa. The fatal termination in such cases is undoubtedly hastened by the damage which the heart has sustained because of the nephritis. In the case of the boy (aged nine years) (cited in Table 14a, Jahrb. f. Kinderheilkunde, I, Folge, Bd. III, 1859), the

nephritis was complicated by embolic gangrene of the lower extremities (thrombosis of iliac vein and artery on both sides).

In the absence of these serious complications, and if death is not caused by the uræmia, the prognosis in these cases of scarlatinal nephritis is, on the whole, a favorable one.

Even in the most severe cases recovery may take place in two or three weeks; occasional traces of albumin are found in the urine for many weeks afterward. The condition may progress to chronicity even when the patient has keen kept in bed from the very beginning of the scarlet fever, but a nephritis extending over a considerable period of time does not preclude eventual recovery.

Frieda W., five years old. Light attack of scarlet fever. Lymphadenitis on the fifteenth day; albuminuria. Two days later, bloody urine. Maximum albuminuria and hæmaturia on the thirty-first day (over two per cent.); then gradual decline. No œdema after the forty-fourth day. Until the seventieth day traces of albumin, although subjectively the patient was well. Patient allowed to get up out of bed on the seventy-seventh day. Discharged on the eighty-second day.

The most disastrous results are met with in those obscure, unrecognized cases of nephritis in which the primary attack of scarlet fever was not diagnosed and the patient has been ambulant for days.

It is impossible to make a prognosis while the symptoms are in the stage of development. Neither the height of the fever nor the degree of albuminuria, nor the intensity of the œdema, are indicative of the ultimate outcome of the case. Of these three symptoms, the degree of temperature elevation is of the least prognostic value. I have cited an instance (p. 298) where the temperature was 40.9° (105.5° F.) in a case of nephritis, and resolution occurred within two weeks.

The *amount of urine* voided during the twenty-four hours gives the best clue as to the progress of the nephritis. The more scanty the amount of urine voided, and the longer the oliguria continues, the more serious is the case. A favorable progress of the nephritis is made evident by an increase in the amount of urine, diminished cloudiness, lessening hæmaturia and reduction in the amount of albumin. Sometimes improvement is inaugurated by a crisis, as in the case of Robert M. (p. 297), where the urine increased rapidly in amount from 150 c.c. to 2000 c.c., and the body weight diminished with corresponding rapidity.

Recurrences seldom occur after complete healing has taken place.

Worthy of special mention are those cases of albuminuria which go unrecognized until after the patient has been allowed to get out of bed. The amount of albumin in the urine is always very slight, and, as a rule, it is possible to free the urine from albumin solely through rest in bed, reminding one of orthostatic albuminuria. The researches of Jehle, Bruck and Nothmann on albuminuria in convalescents justifies the fieble

that the direct cause of this condition is a lordosis of the lumbar spine. This lordosis is the result of a weakened musculature, which, in turn, is caused by the primary disease and the rest in bed necessitated by it. As the musculature becomes stronger, this so-called *"lordotic convalescent albuminuria"* disappears.

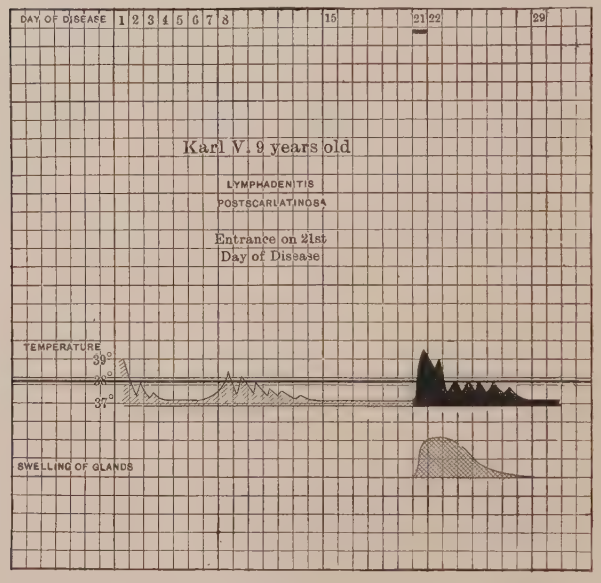
LYMPHADENITIS

A sequel which does not affect the prognosis unfavorably is simple post-scarlatinal lymphadenitis.

Anna H., aged seven years. Moderately severe attack. Temperature normal on twelfth day. Lymph-nodes of jaw enlarged to size of almond.

Twenty-first day: Temperature normal in the morning; 39.2° C. (102.5° F.) in the afternoon. Pain in both angles of jaw.

Fig. 56.



Temperature curve in scarlet fever, complicated by lymphadenitis.

Twenty-second day: Lymph-nodes, size of almond; tender to pressure. Pain disappears in course of day. General condition good.

Twenty-third day: Temperature normal. Lymph-nodes size of bean; not tender to pressure.

With slight elevation of temperature there appears a painful swelling at angle of jaw. As a rule, only one node is involved; it is non-elastic and hard. Subjectively, the prominent symptom is palpation tenderness. The temperature usually rises in the afternoon, seldom exceeding 39° to 40° C. (102°–104° F.). The following morning it falls to 38° C. (100° F.) or below. Further development is subject to individual variations. The general condition of the patient, as a rule, is in marked contrast to the fever. In only a few cases is the condition initiated by vomiting, which may recur. The facial aspect of the child is characterized by marked paleness and puffiness. There is loss of appetite; no restlessness at night. The suspicion of a possible nephritis is aroused, but the urine remains free from albumin.

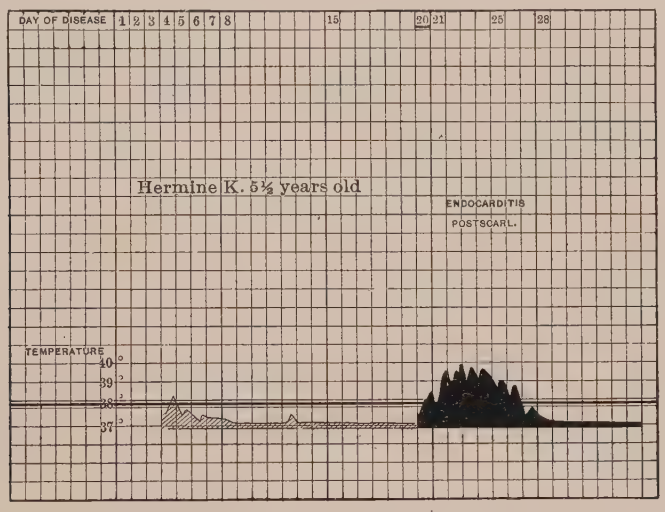
The condition terminates, on the average, from the fourth to the eighth day (Fig. 56). The tenderness disappears first. This is an indi-

cation that the crisis has passed. There is recession in the size and consistency of the swelling; the afternoon remissions in the temperature curve are less marked. The temperature falls by lysis and soon reaches normal. It is rare, indeed, that there is a recurrence, either early or late.

The swelling is seldom of severe grade, and the extensive infiltrations seen in the primary disease never occur. Suppuration is the acme of the pathologic process. It occurred twice in seventy-one cases. It is advisable not to incise until fluctuation occurs.

This type of post-scarlatinal lymphadenitis was present in about ten per cent. of our cases. It occurs about as often as a sequel of scarlet fever as does nephritis. The two affections occur either simultaneously or the lymphadenitis precedes the nephritis. When the latter occurs, the otherwise absolutely favorable prognosis of lymphadenitis is made

FIG. 57.



Temperature curve in scarlet fever, complicated by endocarditis.

uncertain. It is a danger signal, indicating that the ordinarily smooth convalescence from the primary disease is disturbed, and that the course of the sequel is not such an one as would occur under usual circumstances.

The fact that a lymphadenitis has occurred as a sequel or otherwise is of diagnostic value in that it renders it possible to establish the fact that the patient did have scarlet fever. Whenever a child has a unilateral cervical lymphadenitis, without any pharyngeal disturbance, the possibility of scarlet fever should suggest itself. Evidences of desquamation should be sought for and the urine should be examined for albumin.

Leopold W., aged five and a half years. Has a severe lymphadenitis in the left submaxillary region (6 by 9 cm.). Redness of skin over swelling. Examination discloses very fine desquamation on trunk. Careful inquiry elicits information that three weeks before child had fever and eruption.

OTHER SEQUELÆ

Besides the arthritis, of which an example was given (p. 294), there may occur in rare instances temperature elevations, for no discoverable reason, and endocarditis. I have seen five cases of endocarditis. They all followed a mild attack of scarlet fever and led to the development of organic heart disease. The time of onset was the eighteenth, twentieth, twenty-first, twenty-sixth and twenty-seventh day, respectively.

Herminie K., aged five and a half years (Fig. 57). Mild attack. Highest temperature record, 38.1° C. (100.5° F.). Temperature normal on sixth day, continuing normal until twentieth day. On this and following day temperature rose to 39.4° C. (103° F.), with markedly increased heart action. Pulse in evening, 150; temperature, 39.1° C. (102.5° F.). On the twenty-fifth day the hitherto normally situated apex beat was

FIG. 58.

Temperature curve in scarlet fever—endocarditis.

found in the fifth intercostal space. Heart action undulating. Systolic murmur at apex; long in duration. Accentuation of second pulmonic sound. Condition remained unchanged for several days; temperature falls by lysis. On the third day patient is dismissed with a typical compensating mitral insufficiency.

In a second case two febrile periods preceded the onset of the endocarditis; the cause for the rise in temperature remained obscured.

Such elevations in temperature, without apparent cause, may occur at any time during the disease. Interesting in this connection are two cases occurring in one family. Both children suffered from a mild attack of scarlet fever, but had temperature elevations on the same day (Fig. 59).

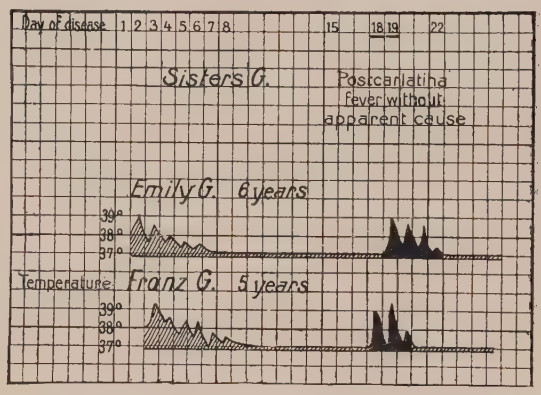
These temperature variations are, however, analogous to those accompanying post-scarlatinal conditions. It is simply a case of not being able to discover the part that is affected. Moser is of the opinion that the fever is caused by an inflammation of the mesenteric lymph-

nodes. Bauer says it is due to absorption of toxins from the intestinal tract. The toxins of the disease paralyze the nerve ganglia of the bowel, peristalsis is diminished and constipation ensues.

I wish now to speak briefly of a number of eruptions which are occasionally met with during the height of the disease. They may consist of large macules and be fleeting in character (Herminie M., p. 295), but, as a rule, the eruption is maculopapulous. In one of my cases such an eruption, of a brownish-red color, was present for several days on the extremities. Each macule at first measured 1 mm. in diameter but rapidly reached a size of 3 to 4 mm. with a small central pustule. Gradual drying.

Lambert M., five years old Mild attack of scarlet fever; temperature normal on seventh day. On the seventeenth day, temperature, 39.5° C.; albuminuria on the eighteenth day. During the succeeding few days moderate fever, with increasing development of the nephritis.

Fig. 59.



Temperature curves in scarlet fever.

Twenty-third day: Commencement of intermittent temperature, between 36.9° C. and 41° C. (98.6° and 105° F.), pyæmic type. General condition bad; collapse; mental confusion; chills.

Twenty-fourth day: Eruption of the type described above. Relapses until the twenty-eighth day.

Twenty-sixth day: Inflammatory exudate in left wrist, right ankle and right knee. Joint swellings continue for an unusually long time. Resolution of the nephritis on the forty-ninth day.

The pyæmic character of the disease at the time the eruption appears leads to the supposition that embolic processes in the skin are the cause of the disturbance.

In the case of a child seen by Heubner, which developed a lymphadenitis on the eighteenth day, and suffered from a post-scarlatinal synovitis, there was present a peculiar skin eruption, consisting of redness and swelling first of the right elbow, then elsewhere on the body, accompanied by pain. On the twenty-eighth day the skin over the right elbow became gangrenous. After this skin had been shed, healing took place. Heubner considered these skin changes as a vasomotor gangrene.

In the past five years I have seen five similar cases, and I have been able to prove that at the time these eruptions were present these efflor-

escences could be induced by trauma (scratching, etc.). I have proposed the term erythema post-scarlatinosum for this exanthem.

Potpeschnigg observed a symmetrical gangrene of both hands in the case of a two-year-old child three months after the onset of the scarlet fever. The condition began during the sixth week of the disease (Fig. 60).

Relapse.—In order to diagnose a relapse, it is absolutely essential and necessary to establish the fact that there was a primary attack of scarlet fever. The diagnosis is justified only when it is certain that there was a characteristic eruption, and in the presence of other signs (angina, raspberry tongue), or when the scarlatinous nature of the disease is evidenced by desquamation, nephritis or the infection of other persons.

Fig. 60.

Symmetrical gangrene of both hands, post-scarlatinal; right hand, child, two years old.

Caroline R., ten years old. Mild attack of scarlet fever. Typical eruption; pharynx red; raspberry tongue; desquamation.

Temperature normal after the fourth day.

On the eighteenth day, reddening of the left tonsil and left anterior faucial pillar. On the former, a white spot the size of a lentil. Patient vomited four times in the course of the day; in the evening, pulse 140 (otherwise 90); angina. On the following morning typical eruption. Spot on tonsil increased in size; pharyngeal reddening more intense. Palpation tenderness of lymph-nodes at angle of jaw. Temperature, 38.5° C. (101° F.) Eruption increased in intensity until fourth day; then receded rapidly. Second desquamation. Recovery.

Relapses have occurred from the eighteenth to the thirty-ninth day (Fig. 61).

The second attack may be much more severe than the first; it may be accompanied by all the complications mentioned, and followed by a nephritis.

Aurelia Sch., eleven and a half years old. Undoubted scarlet fever. Desquamation.

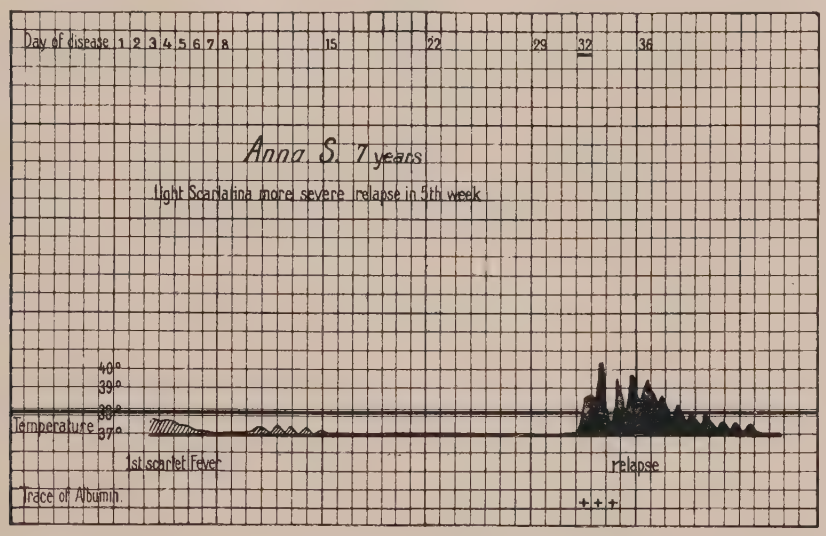
Typical scarlatinal eruption on thirty-seventh day, with angina; joint pains. After convalescence, swelling of lymph-nodes, otitis and a severe hæmorrhagic nephritis on sixtieth day after the onset of the first attack, and twenty-one days after the onset of the relapse.

During the third and fourth weeks of the disease one may observe angina without any eruption, simulating closely the angina of the primary attack. The accompanying temperature curve is also very similar to the original one. In two cases I observed redness and swelling of the pharynx synchronous with a nephritis; in one case angina was accompanied by a synovitis post-scarlatinosa.

A rather remarkable observation, one which may be made in all post-scarlatinal affections, is the occurrence of a symptomless interval between the primary symptoms of the disease and the appearance of the sequelæ.

Older theories as to the cause of the nephritis ascribe this as being due to chilling, irritation of the kidney by food, excessive strain of the

FIG. 61.



Temperature curve in scarlet fever, showing relapse in fifth week.

kidney function owing to the damage done by the disease to the skin capillaries (mechanical theory of Bohn), and to the late excretion of toxins (Leichtenstern). Only the latter theory has met with favor, but it does not by any means account for the occurrence of the other sequelæ. I have come to the conclusion that the real connection between the sequelæ and the primary disease is about as follows:

The exciting causes of the specific sequelæ of scarlet fever (whether the cause of the disease itself or micro-organisms responsible for secondary infections) spread throughout the organism and finally their further development is checked. At the time that the sequelæ make their appearance there is a diminished resistance of the body, or even a hypersensitiveness, and the micro-organisms which have lodged in the various organs of the body are no longer inhibited in their growth. They resume their original activity, and such activity is manifested in part by toxic

and again by infectious symptoms. Then, again, there is the possibility of a reinfection. It must be assumed, therefore, that at the end of the second week of the disease there exists a specific predisposition to post-scarlatinal affections, which continues until about the seventh week. The greatest tendency to a lighting-up of these processes is seen during the third and fourth week, after which time such tendency diminishes perceptibly and rapidly.

Even this theory does not fully explain the genesis of the sequelæ. The conception of a convalescence after scarlet fever must be based on something more than is usually done. The duration of the disease must be conceded to be for a longer time than is indicated by the usual clinical history of the disease. The predisposition to further manifestations, such as the occurrence of sequelæ, must be considered as being a part of the original disease, and complete convalescence can not be said to have taken place until after this period of predisposition has been passed.

PROPHYLAXIS AND TREATMENT

Efforts to effect a cure in scarlet fever must be extended not only to the patient, but also to his surroundings. The well-known conveyance of the disease through the agency of a third person, and the unusual tenacity and virulence of the exciting cause of scarlet fever necessitate the immediate early and complete isolation of the patient. Ideal isolation consists in placing the patient in an isolation hospital, as was pointed out by Heubner.

It is practically impossible to effect complete and consistent isolation in the home. Such isolation is only a half measure, although often this is the only isolation which can be secured in many instances, especially in small cities and in the country. Children who have come in contact with the patient or who have been exposed to the possibility of infection in any way should be excluded from school attendance for at least two weeks, and be kept under observation.

In the case of measles it is useless to resort to isolation after the eruption has appeared, because other children in the family, as a rule, are stricken with the disease several days before the period of eruption. The same is true of all persons who have come in contact with the patient and who have not had an attack of measles. Furthermore, another reason for not isolating these children is the well-known fact that sooner or later children acquire measles. This is not true of scarlet fever, because the majority of persons never contract the disease. The possibility of such acquisition diminishes from year to year, as the natural resistance of the body becomes greater.

The child should be confined in the hospital as long as is necessary, until there is no longer any danger of infection. If removed too soon, the virus is conveyed to the home, where, as is proven by numerous cases

recorded in the literature, infection may occur years afterwards. The virus is highly resistant and quiescence does not imply destruction. The longer the child is kept in the home, the greater is the possibility of infection.

Even when the child is taken to the hospital early, the home should be disinfected thoroughly: Washing the furniture and the floor with one per cent. corrosive sublimate, or five per cent. phenol solution; destruction of the toys. The bedding and other linen should be washed. Clothing should be disinfected with steam; all leather articles should be disinfected with formalin.

The attending physician should arrange his visit to the scarlet fever patient so that it follows the visits made to his other patients; wear a gown and wash his hands thoroughly before he leaves the house or hospital.

In spite of every precaution that may be taken, this is not a guaranty that on the return of the patient to the home, other children in the family will not become infected. The probability for such infection is, however, considerably diminished if precautionary measures are taken.

Worthy of mention in this connection are the efforts that have been made by Russian physicians to prevent contagion by means of the subcutaneous injection of killed streptococcus cultures (Gabritschewsky).

At a meeting of the Science Association held in Salzburg, in 1909, Benjamin called attention to the peculiarly mild course of scarlet fever in children who received an injection of horse serum (diphtheria antitoxin) four to six days before the onset of the disease. He is inclined to ascribe this mild course to the serum injection, and urges that the question be made the subject of further research.

General Treatment.—In every case of scarlet fever the patient should be kept at rest in bed for four weeks. During this period no meat should be allowed.

The necessity for this prophylactic measure has not been established. I am of the same opinion as Ziegler and Baginsky, that the children who were confined in a hospital, and who were treated in this manner, did not suffer from a nephritis to the same degree as did those children who were treated in the home and who were not subjected to these measures.

Withholding meat from the diet is a prophylactic measure based on purely theoretic grounds. I doubt that we are justified in ascribing an unfavorable action on the kidney of the extractives contained in meat and meat derivatives, such as soup and beef tea. It is a matter of observation, however, that children do very well on a meat-free diet, and that in the mild cases there is even a distinct gain in weight.

We do not prescribe a pure milk diet. From the very beginning we allow, in addition to boiled milk, malt coffee and cocoa with milk, milk foods (farina, rice and flour in milk), flour foods (farina mush, milk toast,

cooked rice), then water buns (semmeln), white bread and butter; pea soup, lentil soup and potato soup, cooked or stewed pears and apples.

If milk disagrees with the child, causing nutritional disturbances, we do not hesitate to allow meat (cooked beef and ham) even when nephritis is present. We have never observed any unpleasant symptoms from such a diet.

Alcoholics are shunned, except for use as stimulants in the severe cases. They should never be prescribed for tonic purposes.

Thorough ventilation of the room and the maintenance of room temperature are important. The child should be bathed and its body and bed linen kept clean and fresh. There need be no fear that the child will be chilled.

Baths are not given for therapeutic purposes. The patient is bathed on admission to the hospital, and from four to six baths are given toward the end of the convalescent period. While the disease is running its course, the child is merely washed.

Antipyretics are never used. When the temperature rises beyond 39.5° C. (103° F.) cool packs are employed.

Half of a sheet is dipped into water of a temperature of 15° C. to 20° C. (60° to 70° F.), wrung out and rolled up, the wet half being uppermost. The child is then placed on this sheet, the wet half next to the body, extending from the axilla to the crest of the ilium. Depending on the degree of temperature, this pack is renewed every hour or two, or less often, if necessary.

Another method to reduce the temperature is the following: The child is placed on a dry sheet; a second, wet, sheet is folded so as to cover the chest and abdomen. The dry sheet is then placed over this. This method is a sort of compress and allows of changing the applications more easily.

In the severe cases the temperature and the color of the hands and feet, which must always be kept free for observation, are watched. If the extremities become cold or cyanotic, the cold pack must be removed at once, and if a normal color does not make its appearance promptly, the patient should be wrapped in a dry warm cover. A hot water bottle is placed at the feet, and, if necessary, all along the extremities.

Because of these sudden and extreme variations in the temperature, cool baths are avoided in the severe cases. Changes in temperature and in the extremities are not readily noted, and there is danger of a collapse occurring. Formerly we resorted freely to the use of cool baths and sprinkling the patient with cool water (20 degrees), but discontinued their use when we failed to note any favorable influence on the course of the disease or the condition of the patient.

No treatment need be directed to the eruption or the desquamation. The patient may be anointed with vaseline or vaseline and lanolin. Des-

quamation is hastened thereby, especially when the patient is first bathed in warm soap water. In the hospital we resort to anointing with fatty substances only when the skin is dry, when it itches or when there is a distinct tendency to eczema.

Symptomatic Treatment.—In treating the angina, we must differentiate between the mild and the severe cases. No attention need be given to simple redness and swelling and lacunar deposits. Cold compresses are placed around the neck. These compresses are changed every three hours during the day; at night they are not touched. Older children are given a gargle of any convenient antiseptic (1–2 per cent. hydrogen peroxide).

When the angina is severe, especially in the case of very young children, the mouth should be kept moist and free from mucus, of which there is always a considerable quantity, particularly when mouth-breathing is necessitated because of obstruction of the nares. This is best accomplished by allowing the patient to drink often.

Lemonade, cold tea, tea with lemon juice, are most agreeable to the patient. When the fever is high, we give wine soup. It also serves the purpose of an alcoholic stimulant. It consists of equal parts of wine and water, sugar and the yolk of an egg.

Three or four times during the day the mouth is syringed with cold water. An ordinary ear syringe is used. The child usually objects to this procedure at first, but later the relief obtained overcomes this feeling. The syringing is best done by placing the child between the knees of the nurse, holding its hands and feet, and inclining its head slightly forward.

Other measures are not resorted to, no insufflation of powder into the throat, no painting and no irrigation of the nose.

Ice compresses are not indicated in the mild cases, and in the severe they often are responsible for chilling; therefore, we no longer resort to their use as a means to reduce the fever. Neither is the patient given any ice to suck. When the lips are dry, cracked, bloody and painful, apply a 3 per cent. boric-lanolin-vaseline ointment. The same ointment is applied to the rhagades at the angle of the mouth. In the severe cases these rhagades may be coated. The nostrils may also be smeared with this ointment in cases of rhinitis. This will usually prevent irritation by the nasal secretion. The ointment may be introduced into the nose by means of an applicator, if the child is not excited thereby.

Never try to do too much; avoid polypragmaty. When the child is asleep, do not disturb it, because sleep is as important as any therapeutic measure.

Karl Sch., eleven years old. Severe case of scarlet fever; treated at home. Death resulted because through a misunderstanding of the physician's orders the child was bothered day and night by something or other being done. First, the neck compress was changed; then the

ear was irrigated, the mouth cleaned, the cold pack renewed and the child forced to drink, despite its vigorous protests. Next the medicine was given, and in the meantime the time had arrived to change the neck compress.

If the scarlet fever is complicated by diphtheria, diphtheritic antitoxin should be injected promptly. It is advisable to inject a sufficiently large quantity (3000 units).

If there exist redness and swelling of the tympanum, to be confirmed by examination with the head-mirror, a few drops of a five per cent. carbolglycerin mixture are instilled into the external auditory canal, two or three times daily, and hot or cold compresses (use liquor Burowii), the decision is left with the child, are applied to the external ear. If the tympanum is very red and bulging, and there is pain and high fever, resort to paracentesis. When otorrhœa supervenes, instil a three per cent. hydrogen peroxide solution into the external auditory canal twice daily. If possible, secure the services of a specialist; his assistance is especially needed in cases of mastoiditis.

Swelling of the lymph-nodes is best treated by means of cold compresses. They are efficient, and also relieve the pain of the angina. If the swelling increases in extent or severity, apply a compress saturated with liquor Burowii, paint with five per cent. iodovasogen or apply a ten per cent. ichthyol ointment. Hot applications or compresses (bread and milk or linseed) will hasten the progress of the lymphadenitis to suppuration. Incision is to be resorted to only when there is evident fluctuation, the overlying skin red and thinned out. Inasmuch as the operation is exceedingly painful, it should be done under light ether narcosis. We wish to caution against too early incision. The tissues are infiltrated and secondary infection is exceedingly liable to occur.

The rheumatoid complications do not demand any internal medicine, although aspirin or sodium salicylate may be given. The swollen joints are immobilized and wrapped in cloths saturated with liquor Burowii.

In the severe cases, when the heart is weak, stimulants should be given; internally, digitalis or digalen, black coffee, alcohol (wine soup, tea and cognac, Malaga). Stimulation in these cases is of the greatest importance. Cardiac myasthenia and endocarditis are treated in the usual manner. As a rule, rest in bed is sufficient.

Finally, I wish to emphasize the importance of keeping the bowels well open. I prefer to use for this purpose aqua laxativa viennensis or oleum ricini-syrupus mann., aa. 10. An enema may be given.

SERUM TREATMENT

The excellent results obtained from the use of diphtheria antitoxin have led a number of observers to attempt the production of a similar serum in scarlet fever. Von Leyden made use of a serum secured from

the blood of persons convalescent from scarlet fever. However, the difficulty of getting such a serum makes its use impracticable. Furthermore, the results obtained from its use have been so discouraging as to cast considerable doubt on its efficacy.

The constant finding of streptococci associated with scarlet fever suggested the feasibility of immunizing animals against scarlet fever and to secure from them an antistreptococcus serum.

Marmorek, Tavel, Moser and Aronson have been bending their efforts in this direction. Our experience with Marmorek's serum and horse serum has been entirely negative, but Moser's serum has proven more satisfactory. This is the only scarlet fever serum which has met with any considerable favor. There are few opponents to its use.

In the preparation of this serum, Moser proceeded on the basis that the scarlet fever streptococci are possessed of certain specific properties. He immunized horses, using only streptococci obtained in pure culture from the heart's blood of persons dead of scarlet fever. His method differed further from that of Marmorek and Aronson in that he grew the organism in bouillon without passing it through animals, thus preserving any specific characteristics of which the germ may have been possessed.

The scarlet fever serum differs, further, from diphtheria antitoxin in that horses are injected with a bouillon culture and not a filtrate of the germ. Venesection is done after a month or two; the blood serum is pipetted off and placed in sterile containers—without the addition of phenol.

Disadvantages connected with the use of scarlet fever serum are: (1) the difficulty with which it is obtained, and (2) large doses must be administered to secure any effect. For that reason, too, serum disease occurs not only more often, but is more intense in its manifestations than that which follows the injection of diphtheria antitoxin.

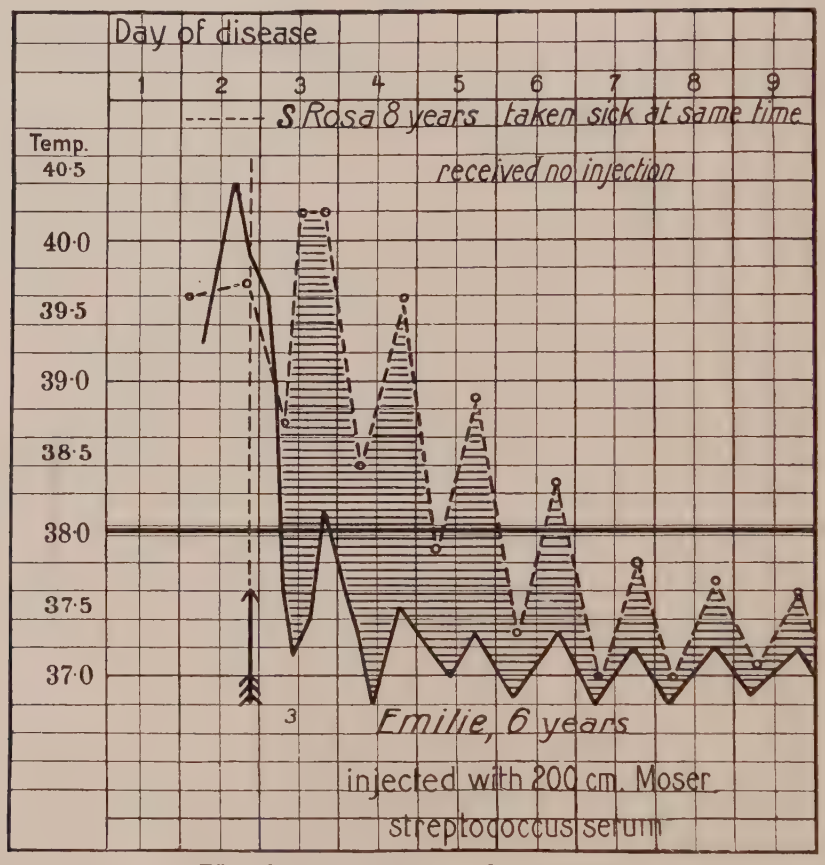
The use of scarlet fever serum is restricted to the severe unfavorable cases, because of these undesirable properties. We convinced ourselves that Moser's serum has a decided influence on the course of scarlet fever. Two sisters became ill with scarlet fever simultaneously, and in the same degree. One was injected with serum; the other was not.

Emilie St., aged six years, and Rosa St., aged eight (Fig. 62), became ill, had fever and an eruption. The following day at 10 A.M. they were removed to the hospital. The eruption was typical; lacunar angina; no complications. Two hour temperature record kept. At 9 P.M., Emilie, 39.9°; Rosa, 39.7°. Emilie received 200 c.c. of Moser's serum. For several hours after the injection, the temperature remained unaffected. At 1 A.M., crisis; 7 A.M., temperature, 37.2°. Rosa had the usual morning remission, the temperature being 38.7°, rising again to 40.2°. Emilie's afternoon temperature was 38.1°; 37.5° on the following day; then grad-

ually going to normal. Rosa's temperature curve was typical, reaching 37.5° on the eleventh day.

The toxic symptoms show most markedly the therapeutic action of the serum—sensorium normal; improved pulse; disappearance of cyanosis and chilly sensations; cessation of diarrhœa. Although one would naturally expect the serum to have a bactericidal action, ameliorating the streptococcic processes, it is in reality antitoxic and therefore

FIG. 62.



Effect of streptococcus serum on the temperature.

is most effective in the pure toxic cases. In order to secure distinctive results from its use, the serum must be injected during the first three days of the disease. After the fifth day the serum loses its effectiveness. The occurrence of complications, especially nephritis, is not prevented.

Only one injection of 200 c.c. of serum is made. The site of injection is the abdominal wall. The puncture wound is sealed with collodion. The injection should be made under the strictest antiseptic precautions.

NEPHRITIS

The mild grades of nephritis do not require any special treatment. We have observed a large number of cases in which no treatment was

given, not even diaphoretics, and found that the œdema and albuminuria disappeared as rapidly as in cases where we resorted to packs and internal medication. Other cases were as protracted in duration with medication as without. Therefore, we have arrived at the conclusion that the course of a scarlatinal nephritis is not influenced by treatment in any way.

It is important, however, to insist on absolute rest in bed. This measure alone controls the albuminuria. It is increased in degree when patients are permitted to walk around too soon. A meat-free diet is enforced as long as there is a trace of albumin in the urine, unless there is established an intolerance to a milk diet, and in the very protracted cases. These are the only exceptions to our rule.

The salt-free diet, instituted in France for the treatment of chronic nephritis, failed to yield any favorable results in our clinic, even as a prophylactic measure. An extensive observation of this method of treatment has convinced us of its ineffectiveness. When nephritis has developed, only the œdema is influenced by the salt-free diet; therefore, it should not be prescribed until nephritis is present.

The method of procedure is as follows: The diet consists of milk, malt coffee, unsalted milk and flour foods, unsalted soup, bread, butter, honey, fresh fruits, stewed fruits, potatoes, etc. (See Vol. I, Feeding of Infants over One Year Old. Also the table in the Appendix, showing Cl. content of foods.)

The complications of nephritis are treated symptomatically. The use of cardiac tonics is productive of good results in cases of heart weakness.

One phase of a severe nephritis demands the closest attention and observation and immediate treatment—uræmia. Delays and remissness in promptly instituting remedial measures may prove dangerous.

When the convulsions become more severe and more frequent, and unconsciousness supervenes, or symptoms of pulmonary œdema appear (severe dyspnœa, foamy sputum), we resort to venesection. Owing to the small size of the cubital veins of children, this procedure is sometimes difficult. We also give a subcutaneous infusion of 200 to 300 c.c. of physiologic salt solution, or high colonic injections of lukewarm water. Hot packs should not be resorted to in uræmia.

We have given up leeching because of the bleeding following the removal of the leeches and the danger of infection when the skin is edematous.

The result of venesection in uræmia is, as a rule, most gratifying. (See case of Robert M., p. 297.)

Gabriele C., ten years old. Moderately severe attack of scarlet fever. Nephritis on the twenty-first day. Twenty-fourth day: Headache, prostration and restlessness, followed by a slight and then a severe

uræmic convulsion. Unconsciousness. Venesection. Withdrawal of 300 c.c. of dark-colored blood. Transfusion of 200 c.c. of saline solution in right abdominal wall. Moderation of convulsions during venesection. After an hour, patient was quiet; slept for two hours and on awakening was fully conscious.

If convulsions again set in, the venesection is repeated.

In the case of Rosa M., seven years old, venesection had to be done three times; 80 c.c. of blood were withdrawn the first time; 100 c.c. the second time, and 300 c.c. the third time. Improvement after each operation; no convulsions after the third withdrawal.

The good results of venesection are by no means certain.

John T., nine years old. Brought to the hospital in convulsions. Died four hours after the withdrawal of 250 c.c. of blood, in spite of immediate stimulation with camphor and caffeine.

It is as yet impossible to prevent the occurrence of nephritis. There is no prophylactic treatment. Even in spite of the greatest precautions to prevent chilling of the body surface, and the most watchful care of the diet, nephritis will occur. So far as our experience goes, so-called prophylactic agents (oleum terebinthinæ, hexamethylenamine) recently come into vogue are useless.

Our statement that every child should be kept in bed for four weeks has reference to uncomplicated cases only. The onset of complications will, of course, make a longer stay in bed necessary. In such cases we keep these children in bed for one week after the temperature has become normal and the urine is free from albumin for a similar period. The diet is increased, a mixed diet is given; the temperature is taken in the morning and at night, and the urine is examined daily. Baths are given freely during this time. Elevation of temperature frequently occurs when the child is allowed to get up out of bed. It is then necessary to enforce rest in bed again for a few days, until the temperature is normal once more. In from one to two weeks the child is allowed to go out of doors.

Although the course of scarlet fever is exceedingly deceptive, unlike measles it is rarely followed by chronic infections; particularly does it not predispose to tuberculosis. Children who do not succumb to the original infection do not, as a rule, suffer from any permanent disability. Eight weeks after the beginning of the disease they are as well as they were before.

The single exception to this statement, one which unfortunately is met with comparatively frequently, is a chronic otorrhœa, with impaired hearing. Functional disturbances the result of damaged heart valves or kidneys occur but seldom.

SIMULTANEOUS APPEARANCE OF MANY ACUTE EXANTHEMATA

The observation of Hebra that the acute exanthemata are antagonistic to one another has been disproved for forty years. Every imaginable combination of scarlet fever, varicella, measles and vaccination has been noted. Such an occurrence is of clinical interest only when these various exanthemata occur simultaneously.

The recognition of varicella is not difficult.

In two such cases we observed the scarlet fever eruption apparently succeed varicella papules—a secondary infection (Huebner); in one case both eruptions were associated distinctly. Pustulation of the varicella papules invariably occurs.

It is far more difficult to differentiate between the eruption of measles and scarlet fever.

Marie Sch., five years old. Entered hospital without a history. On the first day the cheeks only were reddened. No eruption was seen in the circumoral region, although it was not very pale. On the trunk appeared a light scarlet fever eruption. Larger spots were seen on the inner side of the arms, with irregular areas of normal skin. Severe conjunctivitis, coryza, dry cough, typical measles tongue, Koplik's spots. Reddening and swelling of the tonsils.

On the following day the eruption was morbillous, but a grayish-white coating had formed on the tonsils, which eventually developed into a typical scarlet fever angina.

The fever fell by lysis, with simultaneous fading of the eruption; otitis media; later typical scarlet fever desquamation.

We would not advise basing a diagnosis of double infection on the presence of an eruption which might be taken as that of either measles or scarlet fever, because in the case of measles a miliary eruption is often seen here and there on the skin, while in the case of scarlet fever, as has been emphasized elsewhere, a large, morbillous eruption (double exanthem) is often seen.

In the case cited above, the diagnosis of scarlet fever was with certainty based on the angina and the character of the desquamation, whereas the presence of measles was shown by the appearance of the buccal mucosa (Koplik's spots), and the catarrhal inflammation of the nose and larynx.

It is impossible to determine at this time the correctness of Pospischills' contention that the stage of eruption of the exanthemata not only is not deterrent, but predisposes to the occurrence of a second infection.

ROTHELN—GERMAN MEASLES—RUBELLA

BY

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TRANSLATED BY

DR. JOHN RUHRÄH, BALTIMORE, MD.

THE term "Rubella" may be found in medical literature as far back as 1492 but it was not until the eighteenth century that it was used with any degree of frequency by English, French and German writers, and even at that time without indicating any very great confidence in the existence of the disease. Even in the first ten years of the nineteenth century the disease was regarded as a new form of measles, or on the other hand, according to the writings of J. P. Franks, Hufeland and Heim as a special manifestation of scarlet fever, whilst Schönlein considered rötheln as a hybrid of measles and scarlet fever. Wagner, in 1834, published in Hufeland's Journal the first clear description of rubella as a separate clinical entity. Wagner's conclusion did not, however, find many believers and even Canstatt, in 1847, and Wunderlich, in 1854, denied the existence of rubella as a disease distinct from measles. In spite of the excellent work, especially of the German physicians, Faber, Salzmann, Thierfelder, Mettenheimer, Emminghaus and Thomas, the question of the identity of rubella was an open one until 1881. At this time it was discussed at the International Medical Congress, in London, and after long arguments by such distinguished English and American physicians as Cheadle, Shuttleworth, W. M. Squire, Jacobi, J. Lewis Smith, and others, every doubt as to the existence of rubella was dispelled and rötheln was finally separated from measles or English measles, and the term German measles or rötheln appeared in the text books as a distinct disease. In spite of this, some, especially the Hebra-Kaposi dermatological school, held to the older view of Hufeland or of Schönlein, even as late as 1887, in opposition to the important group of pediatrists.

The *contagiousness* of rubella is, according to the uniform agreement of all observers, much less than that of measles and consequently very wide spread epidemics are rarely observed. The infection is usually direct. It appears, however, that the contagious principle can adhere to objects and also to a third person and the disease may be transmitted by either of these means. The source of the infection is generally some

place where children are brought in close contact with one another, as in schools, asylums and playgrounds. Most observers are of the opinion that infection takes place more readily in closed rooms than in the open air, as in closed rooms the conditions for the accumulation of the contagion are better, and many deny the possibility of infection in the open air in ordinary intercourse. This opinion seems to find support in the fact that infection is most frequent in winter and in rainy weather when the children are compelled to remain indoors and when the air of the rooms is in an unusually favorable condition for the transmission of the disease. In closed rooms in institutions the number of cases may reach considerable in a very short time. In Chicago, in 1881, in an orphan asylum in a comparatively short time there were 95 cases; in a New York Deaf and Dumb Asylum, in 1883, out of 450 inmates, 95 were infected and according to the report of Hatfield there were 110 cases out of 196 children in an asylum. The epidemics last according to my own personal experience from 2 to 4 months.

An attack of Rötheln does not protect from an attack of measles or scarlet fever nor does an attack of measles or scarlet fever furnish any immunity from Rötheln. This important fact has been established by thirty years of careful observation and numerous examples, and it can be stated that rubella is a specific disease which is to be separated from the other acute infections and especially from measles and scarlet fever.

Recently (1902) Vitline has reported an instance in *"Wratch"* in which during a short period the same patient had measles, rötheln and scarlet fever. The greatest *susceptibility* to infection is in children from two to ten years of age. Nurslings are seldom affected, Scholl saw a case of intra-uterine infection when the eruption developed a few days after birth. Edwards has noted the occurrence of true rubella in the adult and Seitz has observed a case of the disease in a woman of seventy-three. I have noted it repeatedly in the adult.

The contagiousness reaches its greatest at the height of the eruption and it is my own experience and that of others that at the beginning of the eruption and also when it is fading from the skin there is little or no danger of spreading the disease. According to Thierfelder the contagiousness is greatest whilst the eruption is fading. Owing to the short period of efflorescence the danger of infection is much less in rubella than in scarlet fever or measles, the average duration of the eruption being 3 or 4 days. The nature of the contagious principle is at present unknown. Edwards found a micrococcus in the blood of rubella patients and this he believed to be the cause of the disease but later in 1890 he withdrew his claims for it.

The *incubation* period is on an average of 14 days according to the observations of Thierfelder and Mettenheimer, whilst according to

Thomas and Emminghaus it is from 15 to 20 days. It is certainly true that the incubation period of rubella is an uncommonly long one and indeed longer than that of varicella. The patients do not have any symptoms during the incubation period. Plantegna in his report, in 1903, noted that in the incubation period of rubella as in measles there was a leucocytosis which changed to a hypoleucocytosis on the appearance of the eruption.

A so-called *prodromal stage* is either not observed or lasts but a few hours, rarely 2 or 3 days.

Forchheimer has described from observations in his own family a prodromal symptom consisting of a faintly marked pin-point, rose-red enanthem on the soft palate which had been noted previously by Emminghaus, Thomas and Kassowitz. It is important to note that the valuable diagnostic sign of measles, Koplik spots, have not thus far been noted (except by Widowitz) either in the prodromal or efflorescent stages of rubella. The older writers describe a mild catarrh of the conjunctivæ and of the nasal mucous membranes as a prodromal symptom but this is rather to be regarded as the preceding enanthem period of the exanthematous stage.

According to Theodors, the enlargement of the cervical and occipital lymph-nodes, so characteristic of the stage of efflorescence, may sometimes be seen in the prodromal stage. Koplik has also noted this so-called prodromal sign of Theodors. As a rule there is no fever in the prodromal stage and should there be any elevation of temperature it does not exceed 38.5° C. (101.3° F.). In the United States in exceptional cases there have been several days of more or less severe prodromes.

Symptoms.—The disease is usually ushered in by the appearance of the eruption and by the above-noted symptoms. The eruption is somewhat like that of measles and hence the time honored name "Rubella morbillosa." The eruption generally begins on the head and often on the bridge of the nose and the upper lips, and from these parts it spreads downward very rapidly, reaching the buttocks in a few hours. It is an important diagnostic point that in rubella the eruption is seen on the hairy portion of the head whilst in measles the scalp usually is not affected. On the extremities, the eruption is principally on the flexor surfaces and the palms of the hands and the soles of the feet are also covered. In the beginning the eruption consists of small, point-like, discrete, slightly elevated papules which soon change into oval spots about the size of a lentil, pale rose-red in color, tolerably sharply outlined, scarcely raised above the surface and lying rather close together. In other cases the rötheln spots are irregular with illy defined edges joined by narrow strips of redness which gives the skin a marbled appearance. It is important to note what Koplik mentions in his article in 1900, that the rötheln spots do not become confluent, in contradis-

tinction to the measles eruption. Koplik has also called attention to the fact that the eruption has often a scythe-shaped or crescent-shaped arrangement. In cases where the eruption is smaller than a lentil and the spots very close together it may resemble scarlet fever. These cases in which the characteristic spots are not prominent and the pale red punctate eruption predominates have been called by the older writers "Rubella scarlatinosa." These cases, as I shall explain in the consideration of the "Fourth Disease," should be separated from the others. (See foot note under Fourth Disease.)

It is rare that one sees a rubella patient with all of the symptoms in the same stage. As Trousseau pointed out, it fades rapidly when it is fully developed and so one sees the eruption fading from one part of the body and fully developed upon another. This rapid fading of the rash is characteristic of rubella and furnishes an important differential point in the diagnosis between this disease and measles. The stage of efflorescence lasts scarcely two or three days. The fading of the rash is followed by a rapid disappearance, leaving behind but a transient pale brownish discoloration. The desquamation is trifling. The temperature is elevated during the eruption period but only moderately and it is of short duration. It may rarely happen that the fever is unusually high (Case of Dupres). At the beginning of the eruption the fever is at its highest point or the highest point may have been reached before the appearance of the eruption and when the rash is fully developed the temperature usually falls and the patient is fever-free. The enlargement of the cervical lymph-nodes is usually noticeable during the entire course of the disease. Klaatsch considers of especial importance the enlargement of the postauricular lymph-nodes situated on the upper part of the mastoid process and I have been able to confirm this in a number of epidemics. In describing several epidemics Klaatsch says of this: "This symptom was so constant in the last epidemics that one could make a diagnosis in the dark by means of the sense of touch provided he knew there had been an acute infectious exanthem present." Here and there swelling of the lymph-nodes at the angle of the jaw occurs as well as of the chain of nodes in the back of the neck. Musset noted in some cases swelling of the axillary and inguinal nodes.

During the entire course of the disease the general condition is but little affected and great prostration is not observed. The patient coughs but little and the cough has a tracheal character.

Various **complications** have been noted and of the most important are marked inflammation of the pharynx, bronchitis and bronchopneumonia, acute catarrh of the stomach and bowels, and even choleriform enteritis, and less often multiple serous inflammation of the joints and painful swelling of the thyroid. Of these complications almost all have been reported by physicians in the United States. I do not

remember having seen any of them and it seems that the epidemics of middle Europe are lighter in character than those observed in America.

Rubella vesiculosa is a rare form and analogous to morbilli vesiculosi. Koplik has noted the occurrence of an abortive form in which according to his experience there was nothing except the swelling of the cervical lymph-nodes. He noted in numerous instances such swelling in individuals who had been exposed to rubella infections and there was subsequently no eruption. In these cases the swelling subsided in a few days without any febrile disturbance. I shall not consider Tschamer's so-called "ortliche Rötheln" as I am of the opinion that it has nothing to do with the clinical feature of rubella.

In sporadic cases the **diagnosis** of rubella is difficult, as it resembles mild cases of measles as well as the abortive forms. In epidemics the diagnosis presents no special difficulties and it may be separated from measles by the milder course, the slight febrile disturbance and the absence or mildness of the catarrhal symptoms. The swelling of the cervical lymph-nodes, and the so-called Theodors' prodomal sign are of value and particularly the absence of Koplik spots. If the disease follows a measles epidemic and the patient has had measles a short time before the diagnosis presents but little difficulty. Schmidt has noted that the urine in rubella does not give the diazo reaction whilst in measles this reaction is present. It is interesting to note that antitoxin rashes have been mistaken for German measles.

The **course** of the disease is so mild that the physician has but little to do and the saying "Vix nomen morbi merebatur" applies. The child does not feel ill as a rule and the patient, if an adult, can scarcely believe that he is suffering from an infectious disease.

In most instances the physician is called only to give advice because the parents are afraid that the disease is either scarlet fever or measles.

In the United States epidemics of a severe character have been described and the mortality rate has been as high as from 4–9 per cent. It is possible that there may have been an error in diagnosis in these fatal cases.

There are no especial instructions for **treatment** in rubella. Owing to the mild character of the disease isolation is rarely advisable. Ashby recommends isolation for 3–4 weeks which is too long when the short duration of the infectious period is considered. In Germany the sanitary regulations for rubella are the same as for measles. The imperial Russian sanitary code forbids children who have been in contact with rubella patients to attend school for 16 days and the patient must not attend school until two weeks after the beginning of the exanthem.

DUKES' "FOURTH DISEASE"

BY

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TRANSLATED BY

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THE term "Fourth Disease" is first found in the Lancet of July 14, 1900, in an article by Dr. Clement Dukes, head physician to the Rugby School, entitled "On the Confusion of Two Different Diseases under the Name Rubella." Since then the term has been in use chiefly by English physicians.

Dukes' "Fourth Disease" is a mild affection like rubella but with a rash resembling scarlet fever as the rubella rash resembles measles, or we might say that it resembles closely the abortive form of scarlet fever.

One naturally asks upon what observations does Dukes base his opinion that the "Fourth Disease" exists as a separate clinical entity. In 1892, Dukes was asked advice concerning sixteen cases supposed to be scarlet fever. These cases occurred in a public school and Dukes, having been convinced that a "Fourth Disease" existed, and believing that the cases in question were of this nature, isolated the patients for only fourteen days. Notwithstanding the short period of isolation there were no infections in the families of the children. Dukes relates another epidemic also in a school where thirty-one typical scarlet fever cases were mixed with cases of the "Fourth Disease." The incubation period of the latter was from fourteen to fifteen days whilst that of the scarlet fever cases was but two or three days. In nine cases the patients had first the "Fourth Disease" and then scarlet fever and one patient had scarlet fever first and the "Fourth Disease" later. There were two fatal cases of scarlet fever in this epidemic. Dukes also observed another pupil who had previously had scarlet fever and then the "Fourth Disease." Many of the patients who had the "Fourth Disease" had previously been attacked by rubella. In a third house-epidemic there were nineteen cases of "Fourth Disease" and 42 per cent. of these patients had previously had rubella.

*This chapter has been translated and allowed to remain as originally written. The translator is of the opinion, however, that whilst there may be a fourth disease there has not been sufficient proof of it and he would therefore at least for the present classify all such cases as Rubella. In his experience one of the distinctive features of rubella is the polymorphous character of the eruption, like measles in one case, like scarlet fever in another and like a mixture of the two in others.—J. R.

Owing to Dukes' observations covering years of experience the author considers the "Fourth Disease" as a distinct affection quite independent of measles and scarlet fever. The following account is based largely on Dukes' publications.

Except for trifling pain in the throat the so-called *prodromal symptoms* are wanting in most cases, although occasionally there may be a chill and several hours of nausea, headache, backache and loss of appetite. The incubation period varies from nine to twenty-one days resembling rubella and differing markedly from scarlet fever. The eruption is usually the first indication of the disease and it may cover half of the body in a few hours. The eruption is small and thickly set, pale red and scarcely raised above the surface. This exanthem is also seen on the face but according to Dukes less clearly and not at all on the nose or region of the lips. The pharynx is somewhat swollen and markedly congested. The tongue is coated but the typical scarlet fever tongue is not present. The lymph-nodes of the neck are swollen, hard and about the size of a pea and they do not attain the size of the nodes in rubella. In some cases the axillary and inguinal nodes are enlarged. The eruption fades quickly and is followed by a mild but recognizable desquamation which is complete in about two weeks. Exceptionally the desquamation may be very marked. Nephritis is a rare sequel; but a trifling, rapidly disappearing albuminuria may be observed.

There are few *general symptoms* and the pulse rate is unaffected in the mild cases whilst it varies with the temperature in the more severe ones. The temperature ranges from 37° C. to 40° C. (98.4° F. to 104° F.). Any symptoms that are present disappear when the rash fades. The infectiousness is trifling at the onset and disappears entirely in two or three weeks. The patient is ready to get out of bed in 15 or 16 days; the isolation may be ended in two or three weeks.

I have described the "Fourth Disease" according to the author's account of it and noted how closely it resembles abortive scarlet fever. But, as we have seen, the characteristics of the "Fourth Disease" are its mild course, the absence of complications and sequelæ, the rapid disappearance of the infectiousness and, what I consider of especial importance, the long incubation period.

Dukes' article started a rather lively discussion amongst English and American authors and whilst part of them (W. H. Broadbent, Th. Johnstone, J. J. Weaver, A. Croick, A. L. Millard and Walter Kidd) agreed with Dukes, others (C. K. Millard, A. Rutter, F. F. Caiger, F. J. Poynton, William Watson, J. W. Washburn, Ker, F. C. Curtis, H. L. K. Shaw) thought Dukes' conclusions erroneous and that cases of the "Fourth Disease" should be classed as either scarlet fever or rubella.

The article of J. J. Weaver furnishes the most conclusive evidence. His experience was as follows: Some months prior to Dukes' publi-

cation, he noted in the Southport Borough Infectious Disease Hospital in which he was medical superintendent, in a number of scarlet fever cases, recurrences with a new eruption and fever. In 20 cases of scarlet fever 6 such recurrences were noted in three months. He reported 14 hospital cases in his experience with their temperature charts. These charts are of especial interest because they are in cases in which the "Fourth Disease" either preceded or followed scarlet fever.

The clinical picture of Weaver agreed in the main with that of Dukes. He called attention to the regular fine, punctiform character of the eruption and noted that in his cases the rash appeared first on the face and, contrary to scarlet fever, involved the skin surrounding the mouth. Certain rather negative features he considers characteristic of the disease, little or no fever, little or no disturbance of the pulse, very slight pharyngitis and practically no general symptoms. There was no strawberry tongue, and the incubation was nine to twenty-one days. The mildness of the symptoms of course suggests rubella but neither coryza nor cough was observed, and the swelling of the cervical lymph-nodes was less marked and not so constant as in rubella and lastly, in his cases there was no marked desquamation but a simple scaly separation of short duration.

The existence of the "Fourth Disease" as a separate clinical entity can only be determined by a series of unprejudiced observations but one can state that there exist mild epidemics suggestive of scarlet fever which attack children who have already had scarlet fever and rubella and it does not protect the patient from a subsequent attack of either scarlet fever or rubella.

All of us who have to do with the acute exanthemata either in the hospital or in private practice have doubtless seen such cases as Dukes and Weaver have described. I myself have repeatedly seen such cases but unfortunately have not made such observations as would serve to clear up definitely this question. It must be noted, however, that the observations of Dukes and Weaver, however convincing they may be, do not suffice to solve the interesting and important question. When we search the literature of rubella we find much which in my opinion goes to show that Dukes is on the right track and that his opinions will be verified.

It is remarkable that Dukes, before he published his important studies, did not search the foreign literature for there he would have found much enlightenment upon this subject. In 1885 Nil Filatow, in an article in Russian, raised this question and, in 1896, in his lectures on the infectious diseases of children outlines in a special chapter a separate disease similar to the one which Dukes described. Naturally he did not include under the heading "rubella scarlatinosa" those cases of rubella in which in addition to the typical spots there is an erythem-

atous eruption. According to Filatow, rubella scarlatinosa is "a separate acute infectious and contagious disease, which is characterized by a scarlatiniform eruption but which may be separated from scarlet fever by the mild course and especially by the difference in the contagiousness."

In my opinion megalerythema epidemicum or erythema infectiosum (or the fifth disease, as the latest French writers would call it) which has been a matter of discussion in the German literature since 1900, has nothing to do with the "Fourth Disease" The disease described by Trommer in 1901 as scarlatinois, and that which Pospischil called scarlatinoid have no bearing on the question of the existence of the fourth disease.

ERYTHEMA INFECTIOSUM

BY
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TRANSLATED BY
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Synonyms.—Local rubeola (Tschamer), Megalerythema epidemicum (Plachte), Grossflecken (Plachte), exanthema variabile (Pospischill), erythema simplex marginatum (Feilchenfeld), erythema infantum febrile (Tripke), epidemic erysipelas of children (Tripke), fifth disease.

Historic Note.—Dr. Anton Tschamer of Graz in 1886 described thirty cases. In 1891 Gumplowicz of the clinic of Escherich reported seventeen cases, in 1896 Tobeitz reported some cases at the Congress of Moscow. All these authors, however, regarded the disease as true rubeola or a peculiar type of the disease etiologically identical. During the discussion following the report of Tobeitz, Escherich was the first to regard it as a distinct disease entity. This view was corroborated by his pupil, A. Schmid, who described in detail many points pertaining to differential diagnosis. All cases hitherto reported had been observed in Graz, where erythema infectiosum had occurred in at least four different epidemics during these years. In 1899, Sticker observed in Giessen and vicinity a spread of the disease which he held to be as yet unknown in literature. He and his pupil Berberich are the authors of an excellent description of the disease, who also gave it the name here adopted. Reports then appeared from *Berlin* (Plachte, observations from May, 1900; Feilchenfeld, observations from October, 1901); from Coblenz (Tripke, 1901); from Vienna (Pospischill and Escherich, 1904); from Sölingen (Heiman, 1904); from Munich (Trumpp, 1906); and several reports from Italy, Russia and America. It is a question whether we can class with this disease cases of epidemically occurring "Erythema simplex seu exsudativum" and "roseola æstiva," mentioned by older authors (Gerhardt, Willan, Bateman, Henoch, Kaposi). The disease is not even to-day well known. Even after 1900 many observers regarded themselves as the first discoverers. In German literature we find about 300 cases.

Characteristics of the Disease.—Erythema infectiosum is an acute, contagious, exanthematous, infectious disease causing but slight constitutional disturbances. The leading symptom is a polymorphous maculopapular or confluent erythema (like erythema exsudativum multiforme), involving particularly the face and extensor surfaces of the extremities and lasting with remissions and intermissions at least one week.

Occurrence.—The disease occurs in epidemics of moderate severity (most frequently in spring and summer), also at times sporadically. There seems to be an association between epidemics of this disease and epidemics of scarlatina, measles and rubella. It attacks the young at the age of 2 to 18 years, occasionally it occurs in adults, girls are more

liable than boys. According to statistics it is rare under the age of 2 to 3 years; it is possible, however, that the disease at this age is not always recognized because it may run a different course. As to its geographic distribution nothing definite is known. Sticker's researches for a specific cause have not proved successful.

Contagion; Predisposition.—The appearance of a number of cases in certain localities, city districts, schools, institutions and families has repeatedly been shown, nevertheless it seems that either the contagiousness is not great or there exists but little predisposition. Escherich and Pospischill, who have admitted children with erythema infectiosum to the public wards, have never observed a case of ward-infection. According to Sticker the disease is not transmitted by contact with the patient, and Schmid believes that it is not an infectious poison but an obscure something which affects different individuals simultaneously. According to the writer's observation, however, a patient admitted to the child's clinic at Munich without doubt infected one assistant and he again another patient of the institution. The period of incubation is said to be from 5 to 14 days, this being the interval between the appearance of the first symptoms among members of the same household, although this period may vary. The incubation stage of the cases observed at the Munich clinic lasted at least 7 and not longer than 17 days.

Prodromes are rarely noticed. For a period of a few days (1 to 3) there may be malaise, restlessness, chilliness, slight nasal catarrh, sore throat, earache, slight difficulty on swallowing, very exceptionally nausea, vomiting and photophobia.

Symptoms.—The eruption shows itself first on the face. Isolated, round, slightly raised red spots or pale wheals surrounded by a red border appear on the cheeks. There may be no further change in the eruption, but more commonly the spots become larger and confluent on the second or third day, while the central portion seems flattened and faded. The cheeks (frequently also the ears) appear intensely infiltrated, engorged, red or bluish-red, resembling erysipelas, with a sharp and jagged line of demarcation. Some patients have the appearance of being intensely overheated. The central portion of the face, the lips, chin and bridge of the nose may remain free from the eruption, or somewhat later—likewise also on the forehead, temples and in the region of the throat and neck—there may be seen small efflorescences with but a slight tendency to become confluent.

Then in 1 to 3 days the eruption is also found on the extremities arranged quite symmetrically, the favorite seat being the extensor surfaces of the forearms and legs, shoulders, hips and buttocks, never on the fingers and toes, rarely on the palms of the hands and soles of the feet (two personal observations). The arrangement of the exanthem on the lower extremities is quite symmetrical. While the eruption in these regions also consists originally of pale red spots resembling measles or rubella, they soon tend to change to circular or crescentic or poly-

cyclic figures, forming bright red wreaths and map- or net-like figures. They may give a mottled appearance to larger areas of skin, especially as together with the original hyperæmic redness the rings in the areas of the first eruption present in their central portion a bluish-red, livid or gray and brownish-red tinge. Thus the erythema maculopapulosum changes to an erythema annulare, gyratum, marginatum, figuratum. The diffuse erysipelas-like redness, which, on closer examination, is found to consist merely of a delicate meshwork, rarely appears on the extensor surfaces of the extremities. While the original hyperæmic spots completely disappear on pressure or stretching of the skin, there remain later in anæmic areas yellowish or brownish spots.

Thirdly, frequently not until the third or fourth day, after the exanthem on the face has already subsided, there may appear on the skin of the trunk, neck, chest, abdomen and back, especially on the buttocks, a macular, annular or roseola-like exanthem. Very frequently the trunk remains free from the eruption.

A peculiar characteristic of the eruption is its evanescence. After 2 or 3 days it may quite suddenly disappear only to return again a few hours or days later. While examining certain areas of the skin which seem free from the eruption, it may appear in a few seconds either spontaneously or as a result of irritation (chemic or thermic). The return of the rash does not attack the various parts of the body in regular succession like the first eruption.

As a rule the eruption subsides without causing desquamation, although at times on the trunk there are small flakes or scales detached. On places where the eruption has been most marked, pigmented spots may remain for a while.

In addition to the eruption which often is the only apparent sign of the disease, some cases may be accompanied by the following variable symptoms: Moderate rise of temperature of short duration. By the time the case comes under the physician's observation it has usually fallen to normal or become subnormal. Once the writer observed for two days a temperature of 39° C. (102° F.). Tripke has reported cases in which the temperature rose to 40°–41° C. (104°–105.8° F.). There still remains some doubt, however, as to whether they could properly be classed with this disease.

Slight catarrhal conditions of the mucous membranes are often present, rhinitis, bronchitis, coated tongue, redness and swelling of the mucous membranes covering the mouth and pharynx, angina with a punctate or streaky lacunar deposit, injected conjunctivæ.

The eruption on the mucous surfaces is very slight; Sticker has observed a mottled appearance of the mucous membrane of the mouth, Pospischill an annular, Heiman a macular exnanthem. The writer has twice seen on the fourth day of the disease small petechiæ on the hard palate (also on the skin of the lower part of the face).

The lymph-glands may become enlarged in connection with the

disease, at the angle of the jaw, in the neck, under the lobe of the ear, also on the elbow. Pospischill has found the spleen in all cases more or less enlarged—once or twice among my own cases a spleen tumor was present. There may be pains in the joints, once even fluctuation over the patella is said to have occurred. F. v. Müller reports severe attacks of sciatica. There is a tendency to constipation and the pulse sometimes is rapid and somewhat irregular. In my own cases I have frequently noticed indicanuria. In a four-year-old there was present on the fourth day a polynuclear leucocytosis (27,200). As for complications, Tripke claims to have seen one case of hæmorrhagic and one of catarrhal nephritis.

Course and Duration.—The eruption, which is often the only symptom, may, as already mentioned, temporarily subside and reappear. During these latent stages of the disease, especially in dispensary cases, one may make the mistake of regarding the disease as at an end.

The duration of the disease (according to observation in the dispensary), is said to be 3 to 5 days (Sticker, Berberich); for a longer duration the patient's carelessness may be responsible; other clinicians, myself included, estimate the total duration 8 to 10 days.

After that the disease always or almost always terminates in recovery. It is extremely rare for the disease to run a different, more severe course or end fatally.

The following is noteworthy:

I. The *morbilloid* (resembling measles) type of the disease in children under three years of age according to observations of Pospischill and Trumpp the erythema infectiosum in very young children deviates from the type described above. The younger the patient the more closely does the clinical picture resemble that of measles. The eruption can not be differentiated from that of measles, the catarrhal symptoms of measles are present, so that the diagnosis at first sight is that of measles. Koplik spots, however, are absent, the temperature soon falls to normal after the prodromal symptoms, and, furthermore, annular, net- or map-like figures make their appearance on the trunk and extremities.

II. Pospischill describes another type of erythema infectiosum, the "Scarlatinoid" (probably identical with the Scarlatinois of Tramnier). In place of the formation of rings, there is seen on the trunk, shoulders, buttocks, forearms and thighs a diffuse redness or abundant efflorescences typical of scarlatina, only somewhat larger, while the distal parts remain free. There is no angina. The peculiar (wheal-like) puffiness and redness of the cheeks and the rapid fall of temperature aid in the differential diagnosis.

III. One very severe case with fatal termination is said to have occurred during the epidemic described by Sticker; Halbay reports the case in Berberich's work:

Two sisters came down with the disease at the same time; in the one its course was typical, in the other assumed a grave form (hæmorrhagic), accompanied by persistently high temperature, appearance of

bluish-red isolated and confluent spots, the size of a nickel, formation of vesicles, desquamation, bluish-black discoloration of the skin, swelling of the skin on hands and feet. Finally a black, bloody crust covered the whole body. Death on the twelfth day.

Two cases of Tripke proved fatal, but the erythema infectiosum occurred in patients having pneumonia.

In the *differential diagnosis*, the following diseases are to be considered:

I. *Erythema Exsudativum Multiforme.* From this disease erythema infectiosum differs in that it runs its course as a rule without fever, pain and severe constitutional disturbance, the eruption begins on the face, the back of hands and feet remaining free, it does not become vesicular, bullous or like herpes, is hot to the touch and as a rule does not last longer than ten days and shows no tendency to relapse. Cases belonging to the group of erythema exsudativum may also occur in epidemics (pellagra, acrodynia, erysipelas).

II. *Pityriasis rosea* is accompanied by itching and followed by desquamation, does not involve the face and runs a chronic course.

III. In *scarlatina*, aside from the severe constitutional symptoms, the trunk quite early in the disease is the seat of the eruption. The characteristic punctate rash of scarlatina is perhaps never seen in erythema; the same is true of the desquamation in leaves.

IV. Differentiation from *measles* is easy, when—as is the rule—there is no prodromal fever and absence of the catarrhal symptoms and eruption on the mucous membranes. Another differential point is that the eruption in erythema infectiosum involves the forehead, scalp and sides of thorax either quite late in the disease or not at all.

V. Erythema infectiosum is perhaps most frequently mistaken for *Rötheln* (*rubella*). One distinct feature about the eruption is its marked tendency to become confluent, to form rings and net-like figures, to appear on the forearms and legs before it involves the trunk, where, ofttimes, it is entirely missing. Rubella eruption rarely occurs in large spots and does perhaps never lead to the formation of map-like figures, it remains out only 2 to 4 days and has a period of incubation from $2\frac{1}{2}$ to 3 weeks.

The persistence of the large spots as also the character of the exanthem serve to distinguish it from the "*fourth disease.*"

Nosology.—Erythema infectiosum is a disease *per se*, not identical with measles, scarlatina, rubella and the "fourth disease." Having passed through these exanthemata no immunity is afforded against infection with erythema infectiosum. All observers state that it has occurred in children who previously had scarlatina and measles. Berberich, Schmid and the writer have also seen it attack children who had had rubella. One attack of erythema infectiosum usually confers permanent immunity from subsequent attacks.

Treatment.—Keeping the patient in the room and bed, perhaps on a fever diet, is all that is required.

VARICELLA

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Varicella is still described in most of the text books as a disease which is uniformly harmless, of characteristic appearance and which rarely needs any treatment.

In the past two decades, however, a number of interesting observations have been made which show that the ordinary conception of varicella is erroneous and that there may be complications which threaten life, great variations from the usual clinical picture and, what is of especial importance, it may often be confused with smallpox. The number of these observations is so great that more than mere mention of the most important of them is not possible in the allotted space.

It is impossible to state just how far back the history of varicella reaches. Hesse (1829) cites a number of authors who thought they recognized varicella in the writings of the old Greek, Roman and Arabian physicians but they have not been able to present much evidence to support their views. However, in the writings of Vidus Vidius (1626) and some of his contemporaries (Ingrassius, Duncan Liddle) it is plain the clinical picture of varicella was well known and was differentiated from smallpox. Vidus named the disease *Crystalli* and mentions that the people call it *Ravaglione,* a name which is still used in Italy.

The *history* of varicella cannot be entered into. Suffice it to say that during the next two centuries many authors wrote upon the subject (see Hesse for citations) some claiming and others disclaiming its identity with smallpox.

Amongst those who recognized and described the disease may be mentioned Heberden (1767), Willan (1808), Heim (1809) and Thomson (1820, 21, 22). Hesse (1829) has published the most complete monograph upon the subject.

The disease remained unknown by the great mass of practitioners and it was not until the introduction of inoculation and vaccination that the subject became one of general interest.

In the first decade of the nineteenth century, smallpox was noted in vaccinated persons and it also happened that varicella was frequently mistaken for smallpox. As the opponents of vaccination used this as

an argument in favor of the uselessness of the procedure this little known disease, chicken-pox, was carefully studied and separated from smallpox. The monographs of Willan (1808) and Heim (1809) showed that varicella was responsible for most of the so-called recurrences after vaccination.

In the following decades the idea that varicella was a separate disease gained ground and, in Germany at least, by the forties this was the common opinion of physicians.

About this time the influential Viennese dermatological school under Hebra declared dogmatically that varicella and variola were identical and it appears that physicians generally were converted to this opinion. The great smallpox epidemic of 1870–1873 again brought up the question of identity and a controversy was once more begun the vehemence and pertinacity of which is scarcely duplicated in medical history. As a result of this controversy most physicians have returned to the idea that varicella and smallpox are separate and distinct diseases.

Varicella originates only through infection, but concerning the *nature of the contagion* we know nothing and we can only surmise as to the method of transmission and as to its portal of entry into the body. It is certain that infection occurs easily when a child is brought into direct contact with one suffering from the disease, or when it remains in the same room for a short time. Infection through the air seems to play a considerable part in the transmission of the disease. The tenacity of the poison of chicken-pox is slight and is practically disregarded in practice and thus is just the opposite of smallpox in which the infectious material may be carried great distances and live for almost indefinite periods. Many physicians of great experience doubt if varicella is ever carried by a third person or by fomites.

The infectiousness begins with the appearance of the eruption (Cerf, 1901, and Apert, 1895) and disappears even before the last crusts have separated. The susceptibility to the disease is very general, especially during childhood. Daily experience teaches that when a child is taken ill in a family, closed institution, asylum or school the majority of the other children take the disease even if the child is at once isolated.

Whilst the susceptibility to the ordinary mode of infection is very general, varicella can probably not be transmitted by inoculating healthy, susceptible children; so that the contents of the varicella vesicle and variola pustule differ essentially. At any rate the inoculation succeds only exceptionally under especially favorable, and to us unknown, conditions.

Numerous inoculation experiments were tried during the first half of the last century partly for purposes of differential diagnosis and partly to demonstrate the difference between variola and varicella. (For literature until 1829 see Hesse). The results were generally negative and the exceptional successes consisted in a generalized exanthem and not in a localized vesicle at the site of inoculation.

It is certain in all inoculation experiments that the contents of the varicella vesicles cannot cause smallpox either in vaccinated or unvaccinated individuals

One attack usually confers a lasting *immunity* and exceptions are exceedingly rare. Just as there are individuals who obtain an unusually high grade of immunity through an attack of varicella with marked intoxication symptoms, so on the other hand there are those who get but a slight immunity from a very mild attack and may, therefore, have a second attack These are hardly to be considered under the ordinary rule, however, as the second attack follows closely upon the first. In the older literature instances are found in the writings of Heim, Hüfeland, Canstatt and Trousseau and in the more recent publications of Comby, Blair, Butler, Netter, etc. The interval has been as follows: fourteen days (Vetter, 1860), ten days (R. Neale, 1891), nineteen to twenty-two days in four cases (Dawes, 1903). Kassowitz saw a patient who had two severe attacks with an interval of one and a half years, and Gerhardt treated a child who had three attacks.

The susceptibility is not influenced by the *occurrence of other diseases.* Varicella may be present at the same time as some other disease or may immediately precede or follow it. Varicella is easier to tell when it occurs with some other acute infection on account of the vesicular eruption being much more easily distinguished from measles, scarlet fever or rubella than these are from one another.

In the older literature there are numerous examples of the occurrence of one or two infectious diseases at one time with varicella (le Roux, Reuss, Boehm, cited by Hesse) and in the more recent times the following may be cited: Thomas (1871), Fleischmann (1870), Prior (1883), Lichtmann (1892), Szczypiorsky (1895) Netter (1894), Bery (1898), Heubner (1904), and others in French and English literature cited by Cerf. Observations of this kind are rare when confined to private practice but in children's hospitals such occurrences are not at all uncommon.

The relation of scarlet fever to varicella is of interest and the scarlet fever virus may enter through a varicella pustule. Heubner (1903) noted that when scarlet fever attacked a chicken-pox patient the redness spread from a scratched pustule just as it would from a wound. Pospischil (1904) gathered from his large material that scarlet fever attacked varicella patients particularly in the first stage when the new vesicles were making their appearance. He believes that the majority of general streptococcus infections following measles and varicella are due to infection with scarlet fever. Cerf (1901) has noted that nearly all the varicella that follows scarlet fever is attended by suppuration.

Of much more importance, however, is the simultaneous occur-

rence of varicella, variola and vaccinia, or of the immediate sequence of the same, because the independence of varicella is thus noted. The onset of varicella during or immediately after vaccination is of frequent occurrence. It may be noted at the time of vaccination. Varicella may appear at the same time as variola. Whilst Thomas (1874) neither saw nor believed in this, we have nevertheless a number of unprejudiced observations. Bourland (1894) saw both diseases during a double epidemic and Pages (1902) the simultaneous occurrence of variola, varicella and vaccinia. J. F. Schamberg (1902) saw a case of varicella brought into a smallpox hospital and the disease developed in 33 children with variola. In some cases only seventeen days elapsed between the appearance of the two eruptions. Where the idea of the identity of the diseases prevails and patients with varicella are isolated with smallpox cases, unless the former have been protected by vaccination they will have an attack of smallpox (Lothar Meyer, Steiner, Förster, Quincke, Fleischman, Eisenschitz and others).

Vaccination takes in children who have had chicken-pox and runs the same course as in those who have not had it,—a fact which any physician can easily verify, and there are numerous references to this in the literature of the last half century.

The accidental occurrence of varicella or variola during the course of the disease has a practical significance.

We will now consider the reasons why the two diseases are not identical. As has already been stated, some physicians believe that the two diseases are only differences in intensity of a single disease. We have not room to consider in detail the century long discussion but will give only the important facts which show that the view of the dualists is correct. One should remember that in many of the discussions the views of the dualists were not always correct and some of their claims were not based upon sound observations.

1. Inoculation with the contents of the varicella vesicle always produces varicella and never variola.

2. The occurrence of varicella does not protect from variola or vaccinia and the reverse is also true.

3. The third question which has been discussed at great length is whether a patient with varicella can cause variola in another and this may be answered in the negative.

Varicella is a disease etiologically different from variola but which at times has clinical manifestations greatly resembling smallpox.

OCCURRENCE; MODE OF SPREADING; AGE INCIDENCE

Varicella is a disease which occurs among all races and which never disappears entirely from the larger cities. Large and small epidemics are of frequent occurrence and are most often seen about the time of

the opening of the schools. Nearly all the epidemics are of a benign character but exceptionally there may be numerous cases of nephritis, secondary infections, or gangrene. Unusually wide spread epidemics have occurred, however, in which the disease resembles variola in its course, the epidemic described by Mombert occurring in Kurhessen in 1824 may be cited as an example.

Varicella is almost exclusively a disease of childhood and some authors, Senator for example, have gone so far as to speak of an immunity in adults, and have given this as a point in differential diagnosis. Others state that the disease is of such exceptional occurrence in adults that all cases occurring in grown people should be under the supervision of the sanitary authorities. On this account adult patients with varicella have been sent to smallpox hospitals and have there contracted variola. During the past year there have been such a large number of cases in grown people in places which were previously and have remained free from smallpox that the question of the occurrence of chicken-pox in later life may be regarded as settled.

However this may be, every case of chicken-pox in an adult should be gone into carefully to avoid the possibilities of error. It is especially important to remember that a variola-like exanthem is common in the varicella of adults. Doubtful cases should be handled in the same way as smallpox owing to the probability of its being that disease and the danger of spreading the contagion if it should be.

The **incubation** period is relatively long. In the majority of the cases the eruption appears on the fourteenth day after the infection, sometimes on the thirteenth and more rarely as late as the seventeenth or even the nineteenth day and in some cases the incubation period is given as four weeks.

As a rule the prodromes are unimportant or absent. Thomas and Henoch say that in most cases the eruption is the first symptom and, in fact, one often hears from the most anxious and observant mothers that nothing was noted until the appearance of the eruption. Bohn, Gerhardt, Cerf and many French authors are of the opinion that mild prodromes are the rule. Semtschenke found this to be the case in 808 cases out of 872 but his observations were made in a Russian orphan asylum where hygienic conditions were not of the best.

The **prodromal symptoms** last only one or two days, rarely four or five, and consist of fever, anorexia, restless sleep, general malaise, and sometimes there is pain in the abdomen, vomiting and nose bleed. Pain in the joints and back may be so intense as to suggest variola. High fever is noted in children who usually have high temperature from slight causes and severe nervous symptoms may be met with in some cases. Demme has noted blood in the stools which disappeared with the eruption.

a

b

c

a. Eruption of varicella (3 phases) on the hand and forearm.
b. Glove-like desquamation of the skin of the hand after scarlet fever.
c. Softening of gland after scarlet fever.

The length and severity of the prodromes varies and it must be noted that a patient who has had severe prodromes may have a very favorable and short course of the disease.

In typical cases the *eruption* appears on the scalp and face and nearly at the same time over the body. There are numerous small round spots part of which either remain small or disappear altogether, the remainder enlarge and form papules about the size of a pea. A small vesicle forms on these in the course of a few hours and this may increase greatly in size. The eruption may be seen in all stages on the same patient at the same time. The picture suggests an astronomical map where irregular stars of various sizes are situated close together (Heubner). After a day or less the contents of the vesicles begins to be absorbed and in a couple of days there remains only a yellow-brown or black scab. This drops off in a few days usually without leaving any scar.

As a rule the child's *general condition* is so little disturbed that it is with difficulty that it can be kept in bed. There is usually little or no fever. The first night may be a little restless, the appetite poor and after that the child feels well again.

According to Thomas and Rille there is nearly always some *temperature* even if it be trifling and of short duration, and this may last two or three days or even much longer. The author has observed a case where there was continuous fever for eleven days. There is no regular temperature curve nor does the severity of the fever depend on the amount or duration of the eruption. The temperature does not furnish any differential point between varicella and light variola cases. In variola there is a fever-free period at the time of the appearance of the eruption, this may be wanting however in some cases. On the other hand in varicella the fever may disappear and recur later. Fever due to suppuration has been reported by Désandré (1901) Lanhartz (1897) and Comby.

The eruption causes but trifling inconvenience, but some patients may complain a great deal on account of it, especially that there is something sticking or biting them. Itching may be present in some cases.

Severe symptoms may come on late as well as in the prodromal stage, even death may result. Fürbringer (1896) has reported a case of undoubted varicella when the child died without there being any apparent complications.

The Exanthem.—There is no great difference in the formation of the variola and the varicella vesicle. A light variola may resemble varicella or varicella may exceptionally resemble variola. A single vesicle may resemble variola in an otherwise typical varicella. The varicella vesicle is not as most recent descriptions give it made up of

a single chamber, but of many like variola. Primary umbilication is not infrequently seen but it disappears more quickly than in variola. Secondary umbilication occurs from the drying of the older central part more quickly than the newer periphery.

The contents of the vesicles are not always clear throughout but may be either watery, milky, purulent or even hæmorrhagic and secondary suppuration of the vesicle is not infrequent. The hæmorrhagic and purulent forms of the disease will be considered later. More rarely the vesicle becomes filled with air, which is drawn in through the injured epidermis as the contents of the vesicles is absorbed (Windpocken, Varicella ventosa, siliquosa, emphysematica).

It is incorrect to state that there is no stage of papules and inflammatory infiltration of the skin. In the ordinary course of the disease the physician rarely sees the papules which are not very prominent

Fig. 63.

Section through a twenty-four hour old varicella vesicle, with slightly clouded contents.

and of short duration. Sometimes, however, papules one or two days old may be noted. Microscopic sections show that the skin is always infiltrated even though the redness is scarcely apparent and it is not uncommon for a papule to attain the size of a smallpox papule or vaccinia pustule. In severe cases there are regions of the body on which the skin between the pustules is swollen and of an erysipelatous redness.

The absence of scarring does not differentiate varicella and variola. When the disease is protracted or when there is secondary infection, bad treatment, scratching or constitutional disturbance, the healing may be delayed and there may be destruction of the skin and permanent scarring may result. It may be difficult or impossible to tell these scars from smallpox scars. The number of these scars is seldom great and a tendency to decrease in size is noted as time goes on.

The histologic picture varies. If one chooses typical varicella

vesicles, those in which there is no purulent exudate and about which there is no infiltration, and compares them with the fully developed smallpox pustules, the difference between the two is most marked. If, however, one chooses the varicella-like vesicles from a light case of smallpox and compares them to a typical varicella vesicle or on the other hand compares typical variola pustules with the eruption of varicella varioliformis, one finds no difference. Unna (1894) at least came to these conclusions as a result of his investigations and lately Heubner has expressed the same opinion. By examining the accompanying figure (Fig. 63) kindly lent by Professor Riehl, and comparing it with a section of a variola vesicle, one sees that the processes are of the same general nature and differ only in intensity and duration.

The vesicles appear usually first upon the scalp and face but often simultaneously on the entire body. New crops of vesicles appear from

Fig. 64.

Hæmorrhagic variola in a ten-month-old child on the 11th day of the eruption. Note the eruption in the mouth. (From Corlett.)

time to time so that one finds all stages of the eruption at the same time on the same part of the body. In smallpox the eruption appears first on the face, a day later on the trunk and two days later on the hands and feet. The eruption is about the same size and thickest upon the face and backs of the hands and wrists. In irregular cases of variola the distribution may be as general as it is in varicella and the eruption may appear in crops. In Fürbringer's case (1896), which was the starting point of the last Berlin epidemic, the diagnosis of chicken-pox was made upon the appearance of the eruption in successive crops, on the other hand varicella is seen in which all of the eruption appears simultaneously.

The eruption may all come out in one day but as a rule new vesicles appear the next day. Sometimes there are distinct pauses after which new crops of the eruption appear, and these may be accompanied by elevation of the temperature. Thomas notes a case where new vesicles

appeared after a month's time but one might question whether this was not a recurrence.

It is well known that eruptions may occur in variola before the appearance of the regular eruption especially when there is chemical or mechanical irritation of some part of the body as from garters, corsets and bandages. Similarly the eruption may be thickly set in varicella especially under bandages, from the irritation of discharges in poorly-cared-for children, and in the genito-crural region from the irritation of the menstrual flow. The pressure of clothing sometimes causes such an arrangement of the vesicles as to lead to the appearance of herpes zoster, with which it may be mistaken. Bókay (1892) has reported a case which was treated as herpes zoster and later in the same family there was an outbreak of varicella. Irritation of the skin may cause varicella to run a much more severe course than would otherwise be the case. Désoil (1892) had a case in which the parents of the child, acting on their own authority, gave it a mustard bath in the prodromal stage. The eruption appeared and there were from 500 to 600 confluent vesicles which suppurated. These healed after about six weeks with very serious scarring.

FIG. 65.

Scars around waist in a seven-year-old boy, six years after an attack of varicella. The pressure of the clothing produced a great number of large pustules, while the eruption was slight on other parts of the body.

The number of varicella vesicles is extremely variable. Thomas gives 10 as a minimum number and 800 as a maximum. Sometimes fewer may be noted and a single one may be all that can be found. These cases occur in children's hospitals where there is a house epidemic and where very careful examination of the children is undertaken.

Confluent eruptions may sometimes be observed. In almost every case the confluence of a few vesicles may be noted. There have been numerous reports of cases in which the eruption was confluent in the same way as in smallpox.

The size of the vesicles also varies greatly. In some cases they are the size of a pin head and Thomas and Henoch speak of "miliary" vesicles. The average size is that of a lentil, and vesicles with an average diameter of 10 mm. are not uncommon. They may be the size of a dollar. (Thomas, Demme) and a case was described in which vesicles 10 cm. in diameter occurred (Geddings, 1885). In such cases one has the pemphigus-like or bullous form of varicella which is to be differentiated from the accidental occurrence of varicella and pemphigus at the same time.

Abortive and rudimentary forms of the eruption may be noted in which the exanthem comes to a standstill before vesicles are formed. There may be a simple roseola which disappears. Thomas described this form as Roseolæ Varicellosæ. It may happen that the eruption goes as far as papule formation and then disappears. Gaillard reported an interesting case in which there were papules in the skin and numerous vesicles upon the mucous membranes. These vesicles occasioned great pain.

Fig. 66.

Varicella enanthem in the mouth of a five-year-old girl. Third day of eruption.

The eruption even in mild cases occurs on the mucous membranes but not so regularly as in variola. Comby has made especial studies of the enanthem and finds that it usually begins before the exanthem but sometimes at the same time or after it.

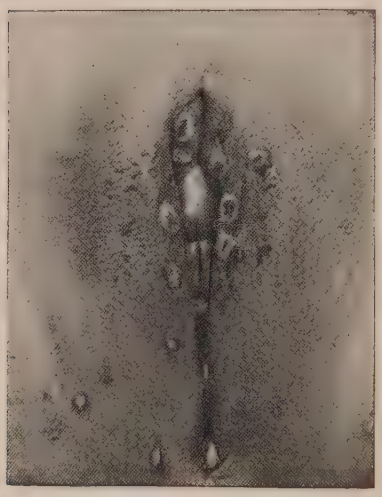
Location.—It is noted frequently in the mouth, on the hard palate, the tongue, gums, and also on the tonsils and pharynx. The number of vesicles is usually small and one may find but a single spot but sometimes the vesicles are more numerous than those of the exanthem. One does not often see the vesicular stage of the enanthem as the eruption seems to develop more quickly in the mouth than on the skin. Usually at the time of the first examination of the mouth the covering of the vesicle has been partly or entirely destroyed by the warmth and action of the mouth secretions and one sees instead of a vesicle an erosion varying in size from that of a millet seed to a pea, yellowish white in color and surrounded by a red zone. These can be differentiated from ordinary aphthæ, when remains of the top of vesicles are still present. These seem to give rise to but little discomfort in most children but some complain on chewing and swallowing. When the vesicles are numerous and inflamed, and there

is a secondary stomatitis, there may be great pain on swallowing, a severe burning sensation in the throat and other similar sensations. Generally the simple lesions heal rapidly and the severer manifestations may be favorably influenced by suitable treatment.

The suppurative infiltration of the ulcerations may be the cause of a severe tonsillitis with fever. Girode (1893) has described a case of pseudomembranous angina due to the streptococcus occurring in the course of varicella. The fever lasted eight days with severe general symptoms and there was a complicating orchitis. Perforation of the soft palate from an ulcerating varicella pustule has also been observed (Kaupe, 1903).

Involvement of the eye is not infrequent and this generally consists of a vesicle on the edge of the lid or upon either the ocular or palpebral conjunctiva. This gives rise to great discomfort and suffering on the part of the patient and may result in a phlegmon of the lid. More rarely the cornea may be involved. This comes on with marked inflammation and in favorable cases healing takes place with a clouding of the cornea. In unfavorable cases, the inflammation extends into the eye as it so frequently does in smallpox. [For literature see Oppenheim (1905) and Cerf (1901)]. It is not unusual for the varicella vesicles to form in the auditory canal. I once saw vesicles in opposite ends of the canal causing occlusion accompanied by great pain, deafness, and tinnitus. Attention may be drawn to the presence of vesicles in the nose by nasal hæmorrhage. Sometimes a purulent inflammation follows and for weeks there may be bloody and purulent discharges which form crusts in the nose and these greatly interfere with breathing.

Fig. 67.



Varicella enanthem about the vulva in the same child. Third day of eruption.

The eruption is more frequent on the genitalia of girls than of boys. In the former it is located on the labia while in the latter it is seen on the glans or prepuce. In boys discomfort is rare (Coombs described a 16 hour anuria) but in girls, vulvitis, painful urination or even anuria may be observed. Through scratching or uncleanliness, ulcers, phlegmons, necrosis, lymphadenitis and even general infection may result.

Of especial importance is the occurrence of the eruption in the larynx and trachea. This has been fully described by French authorities, notably by Harlez (1898) Marfan and Hallé (1896), Roger and

Bayeux (1898) and Lannoise (1896). The symptoms are like those of a severe case of croup, hoarseness, a barking cough, dyspnœa, cyanosis, smothering attacks and asphyxia. Intubation and tracheotomy may be necessitated but sometimes the patient is beyond helping. Cerf collected seven cases, four of which died. The diagnosis in the early stages may be impossible owing to the difficulties of laryngoscopic examinations in young children.

This may be the case where the trouble in the larynx begins before the appearance of the eruption as frequently happens. Without an inspection of the larynx one can never be sure there is not a complicating diphtheria and the early use of diphtheria antitoxin is advisable.

Prodromal rashes are rare in varicella but in some epidemics they may be quite frequent. Henoch has described prodromal rashes resembling scarlet fever coming on several hours before varicella rash. Thomas noted a similar rash fifteen hours before. Fleischmann (1870) observed a measles-like prodromal rash lasting forty eight hours. Cerf has collected forty five cases of prodromal varicella rashes.

As a rule these rashes appear from two to twenty-four hours before the vesicles but rashes simultaneous with or appearing after the vesicles have been reported. At the same time as the appearance of these rashes, or some hours before, there are often high fever, vomiting, diarrhœa, loss of appetite, headache, dizziness, joint pains, and difficulty of swallowing. Burning sensations, itching and subsequent desquamation are not observed. About six-sevenths of the prodromal rashes in varicella resemble scarlet fever, the others are like measles, hæmorrhagic or mixed. The rash rarely covers the entire body and areas of normal skin may usually be noted. The color of the rash is generally a uniform bright red, more rarely either pale or livid red. These rashes last on an average about twenty-four hours, often less, but they may remain for two days or, in exceptional cases, for five or six days. In many cases where there are prodromal rashes there are severe general symptoms or complications.

But few authors ascribe any specific odor to varicella. Heim, however, was of the opinion that it had a distinctive odor quite different from that of variola.

Complications and Sequelæ.—The complications and sequelæ of varicella are rare but nevertheless are as numerous in variety as those met with after other infectious diseases. *Nephritis* is the most important of the complications. This was known from very early times but the first important observations were made by Henoch in 1884. The nephritis following varicella is rarer and more benign than that following most of the acute infectious diseases. There may be little to call attention to the condition and it may disappear without being detected

unless urinary examinations are made as a matter of routine. The cases may be divided into three classes according to their intensity. Unger and later Cerf have made the following divisions: (1) latent nephritis in which there are no symptoms and albuminuria is only discovered when looked for; (2) light nephritis in which there is marked albuminuria and some œdema but no severe symptoms and (3) severe nephritis with fever, marked albuminuria, anuria, cramps, gastro-intestinal disturbances, uræmia, etc.

In certain epidemics nephritis is especially frequent. It is noted usually after the vesicles are dried up and it is important to note that a very severe nephritis may follow a light attack of varicella.

Precautions against nephritis, such as long rest in bed and a milk diet, owing to the rarity of the complication are rarely employed. Children who have previously had nephritis should have all such precautions taken. In all cases where there is nephritis the treatment should be undertaken in earnest as a severe nephritis may otherwise result.

Arthritis varicellosa may occur during the eruptive period or later. It is usually polyarticular but only one joint may be affected. It may start acutely or it may come on gradually. There are two forms, a simple serous form and a severe suppurative form. This last may follow secondary infections by pus germs, or occur through general blood infection or through the lymphatics from some neighboring site of infection. The prognosis in every case must be guarded owing to the danger of general infection.

Complications involving the *nervous system* are much less frequent after varicella than after the other infectious diseases. W. Gay (1894) observed a case of paraplegia with loss of power, sensibility and reflexes of the legs. This occurred in a boy, two and one-half years old, fourteen days after a normal varicella. Recovery took place in three weeks. Under similar circumstances Marfan noted a case of monoplegia which affected the arm and also a case of external ophthalmoplegia of muscular origin. Chorea, multiple sclerosis and encephalitis have also been reported.

Secondary infections with pus-forming bacteria are important. It is not infrequent for most of the vesicles to be infected and become pustules. This may occur in well-cared-for children but more often happens in the weak and poor. Scratching and uncleanliness are the most common causes but crust pustules are the rule in the regions soiled by the urine and stools in uncleanly children. Irritating applications may also cause pustules. The pustules run a longer course than the vesicles, reaching maturity in from 6 to 10 days. They are surrounded by a red inflamed area and in the middle there is a reddish brown umbilication so that it resembles a variola pustule. These are designated by the French as "la pustule en cocarde." Three weeks or even a month

may elapse before the crust falls off. The general symptoms may be severe and these cases may be mistaken for smallpox. Local inflammations as phlegmons, furuncles, subcutaneous abscesses and erysipelas

Fig. 68.

Variola-like eruption in varicella in a two and a half-year-old boy. This case left over 300 scars.

may occur in the course of the disease. General infection may result, with other local manifestations, in thrombosis of the vessels and also severe general symptoms. Amongst other things the following have been reported: osteomyelitis, gangrene of both legs after obliteration of the arteries, suppurative phlebitis of the saphena, suppurative peri-

carditis, otitis media, meningitis, brain and lung abscesses, empyema, and thyreoiditis.

Gangrene of the skin may be observed in the course of any of the acute exanthematous diseases but in none so frequently as varicella. There is much concerning the process which is obscure notwithstanding the fact that the gangrenous form has been known since 1807 (Whitley Stokes), according to Hesse since 1691 (Gideon Harvey), and has been thoroughly studied by many observers. Doubtless underfed, cachectic and tuberculous children and especially those weakened by diseases (measles, whooping-cough, pneumonia and the like) are prone to gangrene, but sound healthy children may be affected as well.

The *bacteriological* investigations have not thrown much light upon the subject. Staphylococci and streptococci are the usual find; but virulent diphtheria bacilli have been noted in a case (A. Krjukoff, 1899), and in Demme's case (1892) the ulcerations were of a tuberculous character.

Fig. 69.

Gangrenous varicella in a two and a half-year-old child. Death on the twelfth day of the disease.

Gangrene may be noted in cases running an apparently normal course, as well as in those which from the beginning show either unusual or very severe symptoms. This complication generally occurs sporadically in an otherwise benign epidemic but sometimes there are numerous cases. Heim (1809) reported that in some epidemics there was an especial tendency to gangrene. The gangrene may begin on the first day (Edwards, 1903) or even as late as the drying up stage. It may affect only one spot or the majority of the papules.

Excluding numerous variations the course is about as follows: Whilst the remainder of the eruption continues its accustomed course some of the spots suddenly become surrounded by a large inflamed area and the contents of the spots become hæmorrhagic. Later the black crusts, which have resulted from the drying of the contents of the vesicles fall off leaving sharp-edged ulcers having a punched out appearance. The bottom of the ulcer is covered with discolored pus or small cheesy masses. The size of the ulcerations varies. They may

remain about the size of a pea, or may enlarge to the size of a dollar or even become as large as a saucer. Enormous areas of ulceration may result from the union of several ulcers and the deeper tissues, fascia and muscles may be involved. Spivak (1895) has described destruction of the scrotum following varicella.

Varicella may predispose to tuberculosis in the same way that measles does. One may see a child with a latent tuberculosis which may be started into an active process by an attack of varicella.

Diagnosis.—This is as a rule easy, as variola is the only disease which causes any real difficulty. Well-marked smallpox cases offer no difficulty, even to those who know the disease from books only, nor does typical varicella cause any trouble, but atypical varicella and the lighter irregular forms of variola, such as occur after vaccination and revaccination, may be impossible to differentiate. The differences have already been fully considered. Of greatest importance are the absence of prodromes and the occurrence of all stages of the eruption at the same time. In doubtful cases there are only two criteria which may be relied upon: The origin of the case from variola and the capability of its causing the disease in others. A doubtful case of varicella should only be regarded as such in the absence of any possibility of smallpox infection. The methods of diagnosis on an etiological basis are unfortunately not of value to the practicing physician.

The differential diagnosis from other diseased conditions must be made but this usually presents no difficulties. All diseases which may be confused with varicella or variola must be considered: Herpes, eczema, pemphigus, impetigo, scabies, varicella, syphilitica, urticaria vesiculosa, drug eruptions, erythema exudativum multiforme and, in the beginning, rubeola, measles and scarlet fever. In all cases the resemblance is a passing one and careful investigation will prevent any mistake.

An exception must be made in unusual cases of pemphigus. Varicella especially in the newborn may cause a well-marked pemphigus, and it may be difficult or impossible to tell this from other forms of pemphigus. The longer duration of the true pemphigus eruption and the occurrence of varicella in other members of the family are points of importance. Sometimes in the papulopustular stage of erythema exudativum multiforme the diagnosis cannot be made for a day or two (see Fig. 70).

Prognosis.—Varicella is usually regarded as such a harmless disease that little attention is paid to it either by the laity or physicians. In spite of the fact that almost all cases, even those with severe symptoms, end favorably, there are still a sufficient number of unfavorable cases which should deter one from giving an unqualifiedly good prognosis. Experience teaches us that weak newborn infants, and those suffering from bowel or lung diseases and above all tuberculous or

scrofulous children may be made dangerously ill by varicella, especially when the patient is living in unhygienic surroundings. Fatalities are rare but may now and then result from the severity of the infection, from the location of the eruption, as in varicella-croup, and from secondary infections or complications.

Treatment.—In most cases treatment is unnecessary. As long as there is fever or new papules appear the patient should be kept in bed. As soon as the eruption has dried and an examination of the urine shows that the kidneys are not involved the child may leave the room.

Fig. 70.

Variola-like papular pustules in a ten-year-old girl after eating decayed fruit.

The fever is rarely so high as to necessitate any drugs directed to the reduction of the temperature. Cooling draughts, cold compresses to the head and sponging with cool water is all that is necessary. If severe brain symptoms come on, lukewarm baths up to five minutes in length, followed by spraying with colder water, may be used.

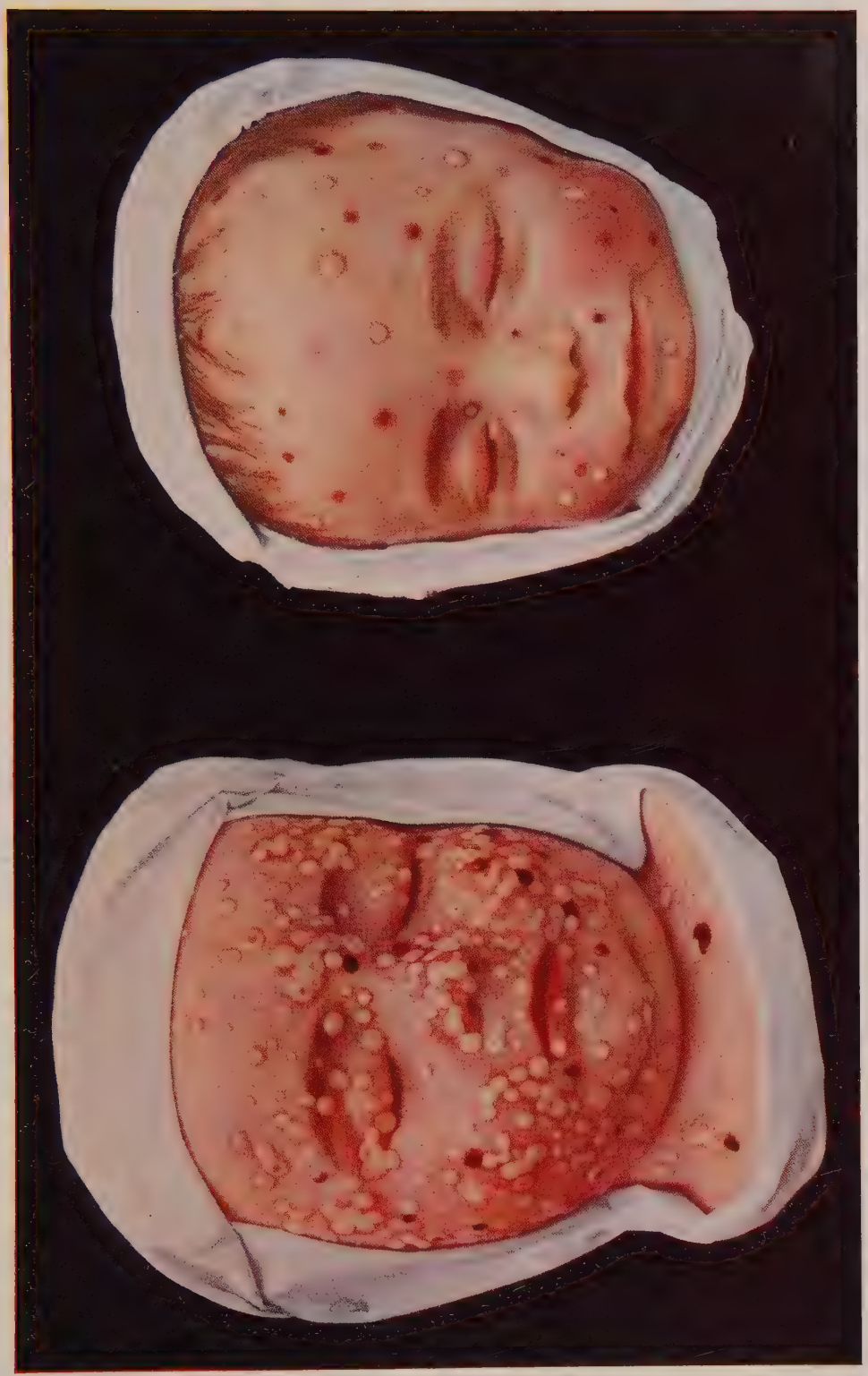
The formation of ulcers in the throat may render some treatment necessary as the pain often interferes with the proper nourishment of the child. Rinsing the mouth with marshmallow tea to which borax or boric acid has been added may be employed.

All solutions containing alcohol, ethereal oils or irritating substances as well as mechanical cleansing of the mouth with a tooth brush should be forbidden. In exceptional cases the pain is so great as to necessitate the painting of the ulcer with a 2–4 per cent. solution of cocaine (followed by rinsing of the mouth).

Great cleanliness should be exercised about the genitalia and if there is any inflammation, ointments containing boric acid or thymol should be used.

Daily baths may be given, but all rubbing and irritation of the skin should be carefully avoided and too hot water should not be used.

Itching, if troublesome, may be allayed by lukewarm baths, fol-



II. Varicella.

I. Variola.

lowed by dusting with some bland powder or by sponging with water to which vinegar or alcohol has been added. Internal medications may be necessary in some cases, antipyrin, phenacetin or even morphia.

The hands should be kept clean and the finger nails should receive special attention. If scratching is not controlled by the child itself the hands or hands and arms should be restrained.

Infections of the skin and abscesses should be treated according to ordinary surgical principles.

The child should be watched during convalescence and if it does not recover its strength, careful regulation of the diet, tonics and even a change of climate may be advised.

Finally, in all cases in which variola is suspected, and in varicella, occurring in adults, vaccination should be practiced.

VACCINATION

BY
PROFESSOR CLEMENS VON PIRQUET, OF VIENNA

TRANSLATED BY
DR. J. P. FABER, SCHENECTADY, N. Y.

THE knowledge that one attack of smallpox affords permanent immunity, for a long time led to experiments aiming to secure the same protection against the disease by means of artificial infection with the smallpox poison.

About the beginning of the eighteenth century, when Europe began to show interest in the matter, accounts from many countries of various modes of inoculation with smallpox appeared. Perhaps the oldest method is the one practiced from the earliest time by the Brahmans. Their technique of vaccination, being much like ours of the present time, is of greater interest to us than the methods practiced in China, Arabia, and the Circassian races.

The external surface of the arm was rubbed with a dry cloth; then with a small instrument, a number of small incisions were made, just deep enough to bring the blood to the surface. Some cotton was then applied which had been impregnated one year previous with the contents of a pustule from an artificially inoculated case.

The result at first was an area of inflammation about the place of inoculation similar to that caused by our present vaccination, and that, as a rule, was followed by a slight smallpox eruption. However, some of these persons artificially inoculated became seriously ill, a considerable percentage of the cases even having a fatal termination. They also spread the disease among unprotected persons.

Because of these objections, this method of inoculation, extensively practiced in Europe about the middle of the eighteenth century, never became generally recognized and fell altogether into disrepute when the value of Jenner's vaccine inoculation became known.

During the latter half of the eighteenth century the observation was made in many places that persons inoculated with cow-pox were insusceptible to the contagion of smallpox. Thanks to the research work of Voigt and others, we now know cow-pox to be an infection of the cow's udder with the smallpox virus from man. It was Jenner, an English physician, who, from 1770 to 1789, on this foundation built up his great system, and discovered the man-to-man method of inoculating the variola obtained from the cow.

Great efforts to extinguish the disease were then put forth on a large scale. As early as the beginning of the nineteenth century, vaccination as protection against smallpox became compulsory in most civilized countries. Later it was learned, that a single vaccination does not confer permanent protection against smallpox, and that revaccination from time to time was necessary. In 1874, the law in the German Empire made vaccination and revaccination compulsory, and consequently all danger of smallpox became practically nil. Other countries stopped half way, some requiring but a single vaccination, others, with consideration for personal freedom, permitted the law to be evaded (England, Austria).

The *cause* of the disease has not yet been determined with certainty. I pass over the enormous literature on this subject, because it has led to no conclusion. This much is certain, that the specific cause, no matter to which species of micro-organisms it belongs, is found very abundantly in the fresh pustules. Its growth on dead culture media has not yet been successful, although we can cultivate it on the skin of man, monkeys, cows, and rabbits, by introducing the contents of a pustule into an abrasion of the epidermis. These cultures result in clinical manifestations which I shall later describe in detail, and after a growth of eight to twelve days they are destroyed by antibodies found in the organism. To prevent its destruction, the micro-organism must be removed from the living (animal) nutrient medium, before the appearance of constitutional symptoms. It may then be kept viable for a long time, either mixed with glycerin or in the dry state.

Inoculation on different species of animals produces marked changes in the virulence of the smallpox organism. The most important practical point is, that having repeatedly been inoculated into the calf, its virulence becomes greatly and permanently lessened, and does not regain virulence by inoculation in man. This reduced virus obtained from the species bovina is called vaccine, from vacca (cow). The most favorable cultural conditions the vaccine virus finds are in its continuous passage through man, from arm to arm (humanized lymph). This method of inoculation carried with it the danger of transmitting diseases of man, especially syphilis. The present method, therefore, for obtaining the virus in great amounts is never by direct inoculation from man to man. In most institutions a calf is inoculated with the virus obtained from man, and from this calf many other calves. The lymph from these calves is put on the market as animal lymph for vaccination of man.

The *virus* (obtained in commerce) is not a pure product of the specific organism of variola, but in addition contains pathologic products of the inflammatory process of the calf's skin. It is obtained in the following manner: A number of incisions on the shaven skin of the calf's belly are infected with the vaccine. After a week, the pustules,

which have formed in these places, are thoroughly curetted with a sharp spoon. The mass thus obtained constitutes the raw material; then the calf is slaughtered and only when at autopsy no general disease is found is this raw material used. Four times its bulk of 80 per cent. glycerin is added to the raw mass, then it is kept in a cool room for a month. The mixture is then rubbed into fine particles and again allowed to stand from one to three months, when it is inclosed in the well-known lymph capillaries. During this time the glycerin destroys other bacteria (staphylococci) while the vaccine organisms remain intact.

FIG. 71.

Vaccinia in the calf from human inoculation.

The vaccine may be introduced in any part of the external skin, although the most favorable location is on the external surface of the upper arm, a method, as mentioned above, early practiced by the Brahmans.

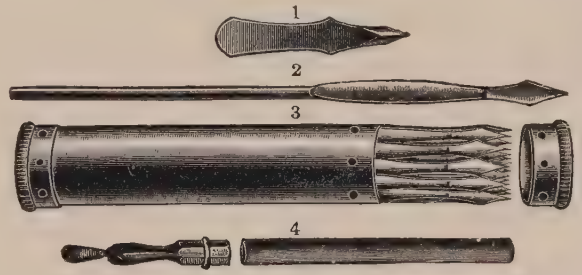
In order to avoid a vaccination scar on the arm in girls, they may be vaccinated ten centimetres below the nipple (Flachs, Schlossman), or on the legs. The latter method is to be advised only in small children who are not able to walk, older children (revaccination) often scratch or soil the vaccination areas.

The *technique* of wounding the epidermis is also of minor importance. It is advisable to make the vaccine wound not longer than 1 cm. and never draw blood.

Plunging needles into the skin, a method at one time much employed, does not give good results. I would advise the inexperienced to make a number of small superficial crossed incisions with a lancet. The experienced operator will accomplish more by making a fine incision with a lancet covered with the virus. Very beautiful round pustules result from boring with a chisel-like lancet, in the same manner as is done in the cutaneous tuberculin reaction method. Surgical cleansing of the skin is not necessary. Most physicians insist that children brought for vaccination be well washed. I merely cleanse the area of vaccination with a little ether.

After vaccination I let the children sit with the arm exposed for ten minutes, and then allow them to dress. I tell the parents to carefully wash the arm at bedtime, in order to prevent the spreading of the virus to other parts of the body where it might produce vaccinia. I do not think it necessary to apply a bandage to the vaccinated area. A tightly fitting bandage is even harmful to the subsequent development of the pustule, causing maceration and hindering the normal process of desiccation. The method of Paul, however, seems to be quite rational. A small amount of Tegmin is applied to the wound and sealed with a small round piece of pressed cotton.

FIG. 72.



1.—Lancet. 2.—Weichardt's vaccination needle. 3.—The same in case. 4.—Lindenborn's platino-iridium lancet.

The scars of cutaneous vaccination and the danger of external transmission of the virus would be avoided by subcutaneous injection. This method has been studied by many authorities and quite recently worked out by Knoepfelmacher and Nobl. They inject 1 c.c. of virus, diluted with 200 parts of normal salt solution, having first determined by means of bouillon culture that the virus is free from pathogenic bacteria. While its results seem to be satisfactory it has not yet to my knowledge been generally adopted. The advantage of vaccinating under the influence of red light and the subsequent protection of the pustule from exposure to all kinds of light except red rays is without scientific basis, as the course of the process is not modified.

When shall children be vaccinated? For the first vaccination, the period between the third and twelfth month of life is the most advisable. If possible it should be done at a time when the children enjoy perfect health, as the fever accompanying vaccination tends to weaken the child. Children with marked eczema should not be vaccinated, because of the danger of infecting the eczema. There are, however, no absolute contra-

indications; if there is danger of smallpox, vaccination is indicated regardless of anything. In cases of children with eczema, care should be taken that the wound is washed a few hours after vaccination, and that scratching is prevented at the time of the development of the pustule.

As for the season of the year when the child should be vaccinated, it is a matter of indifference.

How many scarifications shall be made? The German law on vaccination orders four incisions. The duration and degree of immunity do not seem to depend on the number of foci of infection, any more than does the intensity of the fever. However, inoculating more than one place gives greater assurance of successful vaccination, especially if the physician is inexperienced.

Fig. 73.

Vaccination bandage.

The clinical picture of vaccination in a healthy child is fairly uniform. Deviations in some cases may be but slight.

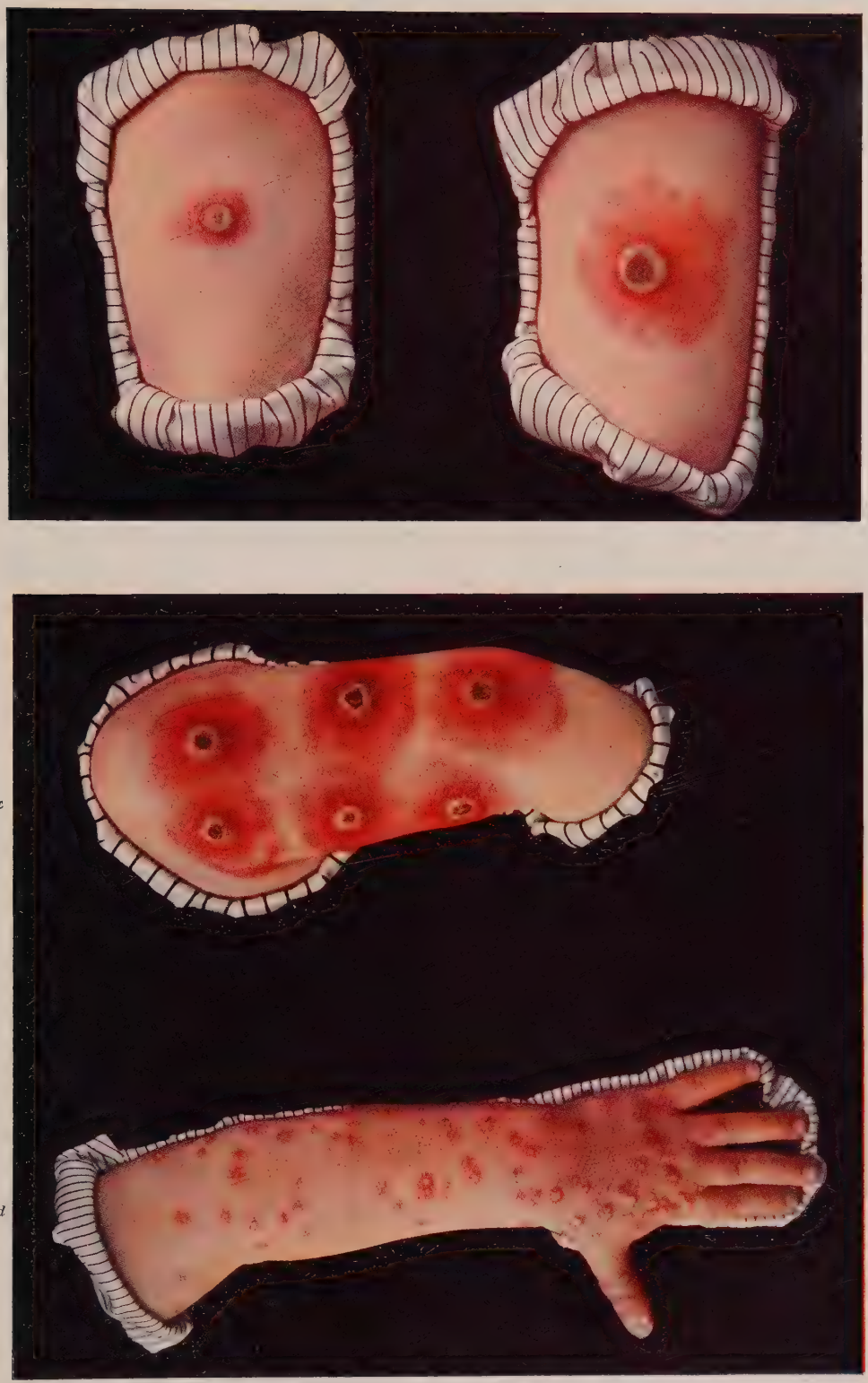
First Stage.—Latent stage.

The effect of the specific infection with the vaccine virus is not visible at once. At first we notice but a slight change, the result of mechanical irritation of the skin, "*traumatic reaction.*" The site of vaccination, after a few minutes, appears red and on stretching the skin somewhat faded in the centre, as in urticaria, the prominence of the wheal depending on the sensitiveness of the skin. In a few hours, we usually observe a redness of 3 to 4 mm. in diameter, which disappears in the course of the day. On the following day there may be seen a small brown scab, surrounding which the skin may be slightly or not at all hyperæmic.

Second Stage.—The development of the vesicle. In two to four days, the specific process becomes visible.

Caroline L., aged five years, vaccinated on the 12th of January, 1907, in six different places on the left arm; two places showed no reaction, the other four developed beautifully. The diameter of the local effect of vaccination measured at least once daily.

PLATE 20.



a and *b*. First Vaccination in an Infant.
a, 8th day. Papule and aula before the appearance of the areola.
b, 11th day. Papule and areola.

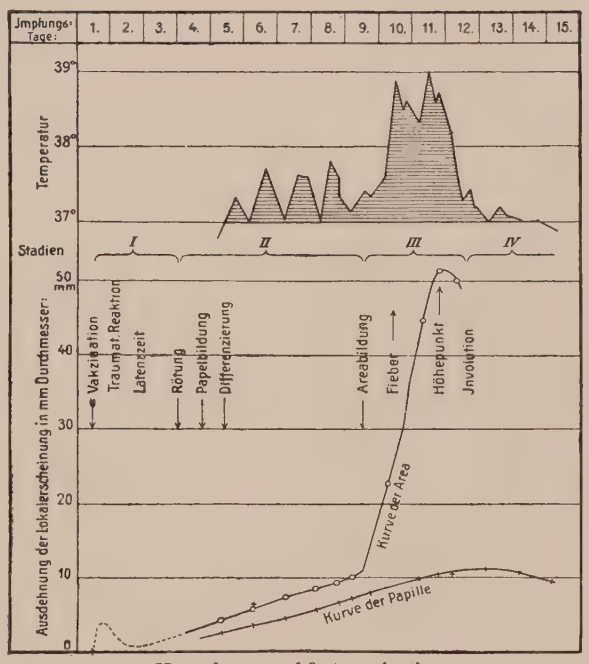
c. First Vaccination in a 2-year-old Child.
11th day. Most intense areola.

d. Cowpox. 15 days after inoculation.

Explanation of the Curve.—Below is the body temperature, which at first was taken twice, later four times daily below the development of the local efflorescences. The curve of the papule is based on the average of the diameters of the four papules, the curve of the *areola* on the diameters of the total hyperæmic zones.

The spot not infected for the purpose of control shows merely a small brown scab without any reaction surrounding it, there is seen at the points where vaccination has taken place a slight redness which in twenty-four hours is plainly raised as a papule above the skin surface. After another twenty-four hours, the differentiation between papule and aula is apparent.

FIG. 74.



Normal course of first vaccination.

The centre of the papule becomes conically elevated and slightly faded, resembling normal skin in color, while the edges of the papule become flattened and retain the bright red color.

Now a uniform growth of the papule begins, increasing from day to day, about 1 mm. While it is at first difficult to distinguish it from normal skin, it gradually assumes the character of a small vesicle. On puncturing, there exudes very slowly a clear lymph, containing abundant virulent vaccine organisms which may be utilized for further vaccination. At one time this "Jenner's vesicle" was used to obtain the humanized lymph.

The papule is not round but depressed in the centre (umbilicated), the edges appearing prominent and well-defined in the surrounding zone of redness, "*the Aula.*" As the papule develops, it pushes out the red ring, although it does not get broader until the

Third Stage.—The development of the *Areola.*

The red border begins to spread, the whole surface becomes infiltrated, appearing as a red plate of 40 to 80 mm. diameter, bearing the papule. After two or three days, the middle zone of the areola begins to fade, the inner zone surrounding the papule becomes pigmented while the outer zone stands out as a red border, but disappears a day later. Then commences the

Fourth Stage.—Involution.

Of the areola only the pigmentation remains, and a slight hyperæmia near the papule. During the development of the areola, the papule (owing to the invasion of leucocytes) assumes a yellowish-white color. The vesicle becomes a pustule or pock. Now it begins to dry, at first in the centre, spreading from day to day toward the periphery, while the growth of the pustule is arrested. It gradually dries up altogether, and the brown scab falls off after about ten days (20 to 28 days after vaccination), leaving the well-known vaccination scar.

If the pustule has been broken by scratching or becomes macerated by dressings, it usually takes longer for it to heal, undoubtedly because of secondary infection.

The *body temperature* in the first stage is not affected. There are slight elevations to 38° C. (100.5° F.) in the second stage. In the third stage, as a rule, fever is present from 38° C. (100.5° F.) to 39° C. (102° F.). This fever is a part of the vaccine infection. It does not depend upon any impurity of the virus, and can in no wise be prevented. Vaccination is not accompanied by temperature except occasionally in the newborn and very anæmic children. Among older and robust children it rarely runs its course without fever. The general condition is, as a rule, only in the third stage somewhat disturbed, corresponding with the height of temperature; there is malaise and pain in the infected arm, depending on the degree of local inflammation. As the vesicle is forming, the axillary lymph-glands become somewhat enlarged and are for a while palpable and slightly painful on pressure.

According to the careful observations of Sobotkas, vaccination produces a polynuclear leucocytosis, appearing in the second period and rapidly disappearing on the seventh to the eighth day, often falling to below normal. This depression lasts three to five days and is again followed by a slight leucocytosis.

A thorough knowledge of the conditions as they appear a week after vaccination is of great importance to the physician. He then sees the development, at the close of the second or beginning of the third stage, of the umbilicated papule with a narrow red border or the commencing areola. At this time a slight rise in temperature is the rule, and it is important to know that the real vaccination fever and the more marked local inflammatory symptoms appear later.

Treatment.—The different forms of medication with purgatives, extensively practiced in olden times, are unnecessary. Nothing should be done for the fever. If the vaccination wound is scratched open, it is well to daily change the shirt and apply a dry powder (Zinc oxide 10.0, Talci 100.0) in small amounts to the wound. If the sores should suppurate longer than eight days (as a result of secondary infection), it is advisable to apply one per cent. peroxide of hydrogen followed by some bland ointment on a piece of linen. The dressing should be loosely

fastened to the arm. Firm bandaging is harmful. The normal pustule which has not been scratched open does not need a bandage. The bathing of the children should be done cautiously between the eighth and fourteenth days to prevent maceration of the pustule. Bathing should be omitted in case the broken pustule is discharging.

DEVIATIONS FROM THE NORMAL COURSE

The duration of the vaccinia depends to a certain degree on the intensity of the infection; the more virulent the virus, and the more numerous and larger the incisions, the more rapid is the course through the various stages. The use of diluted or old virus, which is reduced in strength, or small incisions causes the process to be prolonged for two or three days. (Nourney.)

I have classified one hundred and thirty-nine cases of Nourney and myself, according to the appearance of the height of vaccinia (the end of the third stage) and the intensity of the infection.

Height on	7th, 8th,	9th, 10th,	11th, 12th,	13th, 14th, day.
From intensive vaccinia in per cent. of inoculated...	1	75	24	.....
From vaccinia with diluted lymph, few points by inoculation.....	.....	6	71	24

From this simple retardation of the process for two or three days, we must distinguish the abnormally prolonged period of incubation, which, in my opinion, occurs when the bacteria enter the skin at a point which is unfavorable for their development. It is only by some mechanical irritation or the normal development of vaccinia performed later, that these "dormant bacteria" are awakened.

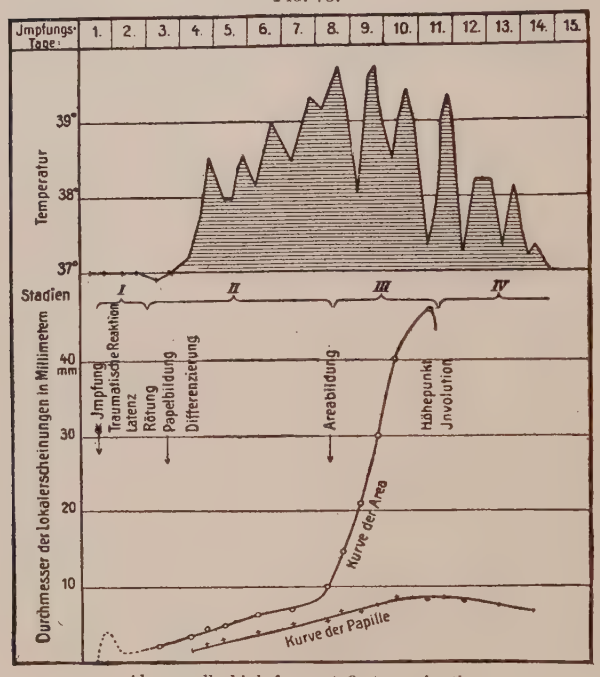
It was known to Sacco that the points of vaccination may remain latent for thirty days and that revaccination brings about their development. If one week after vaccination no result is seen, it should not be taken for granted that the child is immune against vaccinia, but should be revaccinated. I have never had a case in which careful repetition failed to produce a reaction of the first vaccination. It seems, however, that in certain cases the skin has a tendency to render the bacteria inactive or dormant. For example, in a child with myxœdema, vaccination had to be performed three times before it proved successful. Of sixteen incisions only four developed normally. One was negative, while the remaining were inactive until awakened by the development of the normal points of vaccination.

Not infrequently only a certain number of inoculated points lie dormant. They begin to develop a few days after those which have reacted normally and their course is much like that of post-vaccination. A small areola forms around them at the same time as around the pock which appeared earlier.

Accessory or Secondary Pocks.—In the third stage of vaccinia there appear in some cases within the areola, nodules of 1 to 2 mm. in diam-

eter, in one to two days they develop into umbilicated pocks, and dry up together with the original pustule. This phenomenon is of special interest as it reminds one of the inoculation with a mild virus, where it always occurred. The accessory pocks bear a certain relation to the virulence of the lymph. They do not affect the course of vaccinia and as a rule leave very superficial scars. Of greater clinical importance is the cow-pock, or vaccine exanthem, a general eruption which is a rudimentary form of the pock exanthem. After variola inoculation the general pock eruption appeared in the fourth period as the temperature began to fall, ten to thirteen days after inoculation. The individual efflorescences develop into real umbilicated pocks, followed by a secondary fever period. Similar general eruptions are quite frequently observed when using a fresh variola vaccine, obtained after the variola culture has passed but once through the calf. It is extremely rare for a well-developed variola-like exanthem to follow the use of our vaccine, which is obtained after many passages through the calf.

Fig. 75.



Abnormally high fever at first vaccination.

Not infrequently, however, rudimentary forms are seen on closely observing the course of vaccinia, resembling the original eruption only in time of appearance (fourth period), and to a certain degree in localization (extensor surfaces, face and back), while the outline of the efflorescences is very indistinct.

Personally I have observed thirty-two cases of general exanthem following vaccination, twenty-one of which occurred between nine and eleven days. In one case closely resembling variola, there were seen covering the entire body virulent, partly papular, partly vesicular efflorescences. (See the colored reproduction.) In the majority of cases the exanthem resembles that of measles. The papules, however, are harder, and the mucous membranes are free from the exanthem. For a few days new crops appear, and the originally yellowish-red color of the papule gradually fades. All symptoms disappear at the end of a

week. Aside from itching, there are no subjective symptoms, and no rise of temperature.

Eruptions appearing later (about the fourteenth day) resemble lichen, and are usually regarded as an accidental appearing of lichen urticatus.

There is no treatment necessary in vaccine exanthem; if the itching is annoying, apply some powder or a solution of menthol. Abnormally high fever is not so infrequent. It is especially apt to occur in robust older children. It may then, as illustrated below, begin as early as the second stage. It need, however, not cause alarm; only when the temperature does not decrease in the fourth stage should we think of the possibility of secondary infection (erysipelas, or more often measles or varicella, acquired from other children at the time of vaccination).

Cachectic Reaction.—A rather sluggish reaction is apt to follow vaccination in anæmic or cachectic children. In these cases, the papule develops slowly, while there is no hyperæmia at all or but faintly apparent for a few days. The areola appears later and the papule becomes broader than usual, and ordinarily in these cases there is but a slight rise of temperature.

Revaccination.—Repeating the inoculations for a number of days in different places, we can ascertain the action of the vaccination and study the relations of immunity. The first revaccinated places develop slowly in the same manner as at the primary site, but as soon as the first vaccination reaches the third stage the areolar hyperæmia at the same time surrounds all papules, and all become yellow and dry up simultaneously. The places inoculated later differ from the first only in size, as their development is retarded and they are much smaller. When the primary vaccination has reached the third stage, subsequent vaccinations do not reach the stage of papule formation. They show the early reaction. Without a latent stage, there appears within twenty-four hours a small insignificant papule which soon disappears. The same phenomenon is observed, as a rule, when we revaccinate a few months after the first vaccination. In order to see the faint reaction, the site of vaccination must be inspected after twenty-four hours. By the time of the customary inspection (after seven days) it has entirely disappeared. Clinically, it is of no importance but of great pathological interest, as it explains the nature of vaccinal immunity, which consists not in an entire insusceptibility to vaccine virus, but in an immediate destruction of the same.

The organism, which after the first vaccination permitted the virus to develop and destroyed it after a period of eight to ten days (about this time the virulence of the vaccine vesicle disappears), now suppresses the disease in its very beginning, and removes the small amount of foreign bodies without any constitutional disturbance, while in the case

of first vaccination, especially of variolation (inoculation of smallpox) the micro-organisms have become greatly multiplied, before the fight begins.

The immunity which vaccine affords against variola apparently depends on the same principle, namely, that the virulent variola micro-organisms invading any mucous membrane are at once attacked and destroyed before they have multiplied.

The degree of early reaction depends on the dilution of the lymph, while the degree of the first reaction does not depend on the material used. In revaccination, the greater the dilution of lymph, the less marked are the local symptoms, while in vaccination for the first time, the development is only temporarily protracted but not quantitatively retarded. One vaccination changes the reaction of the organism toward the subsequent infection with vaccine or variola during the entire life. The organism attains a permanent *allergy* (*allas* = different, *ergeia*, meaning reaction). A few years after the first vaccination, however, the protection is, as a rule, not sufficiently marked to destroy the infection within twenty-four hours, a few days being required by the organism. The longer the period after the first vaccination, the more frequently do we meet with forms of vaccinia which, in the beginning, resemble the first vaccination but run a rapid course (accelerated reaction). Here also a vesicle is formed, passing through the same stages as the papule of first vaccination. The hyperæmic zone, however (the aula), is generally irregular from the beginning, does not develop so rapidly, so that a sharp differentiation between the second and third stage becomes difficult, but the growth of the papule is completed earlier than that of the first vaccination, the retrograde changes more rapid, the exudate more superficial, so that the scars following revaccination are, as a rule, quite faint. The areola does not attain as great a diameter, although the physician is often led to regard the areola formation in revaccination as especially marked, owing to the fact that on the customary day of inspection (eighth day) he finds the accelerated revaccination at the height of development, comparing it with the appearance of the first vaccination which is still in the second stage and does not develop its full areola until a few days later. Occasionally, however, a very widespread hyperæmia is observed over the entire arm, especially in revaccinated adults, so that erysipelas is often suspected. The reason for this great susceptibility of certain people is not well understood.

The legal question as to whether revaccination has been successful or not can not accurately be answered, owing to the great variation in revaccines. Thus the statistics of different observers vary greatly. A positive reaction in the sense of a pathological process follows almost each revaccination. The question should be: Has revaccination afforded a renewed protection? When on the day of inspection no reaction is

seen, the vaccination may not have taken at all, or the immunity was still so great that it produced a premature reaction. Renewed protection can only then be expected when revaccination is followed by the formation of a distinct vesicle, so that at the time of inspection there is seen a pustule or a scab, surrounded by a reddened or pigmented border.

Fig. 76.

Auto-inoculation after vaccination associated with eczema of the face. Two-year-old child.

Fever does not occur with premature reaction. With accelerated reaction, it is usually but slight and transient. Subjective symptoms consist in itching and pain in the wound, which seems greater than among the first vaccinated, because the revaccinated are capable of expressing their discomfort.

In my experience, accessory pocks and general eruption never occurred with revaccination, but swelling of the lymph-glands and pain occur among the revaccinated adults more frequently than among children vaccinated for the first time. Whether this is dependent on the effect of vaccine or other conditions, is not well understood.

Complications of Vaccination.—The formation of accessory pocks in the areola and cow-pox exanthem about the tenth to the fourteenth day can not be regarded as complications, but are really a part of the process. Complications are vaccinal infections of the individual from himself or from his surroundings; also secondary infection caused by the lymph or carried into the wound later. By far the most frequent complication is caused by the children wiping off the lymph, which is usually found around the area of vaccination, with their fingers and inoculating other parts of the body. At each of these places, there develops a regular vaccinia, passing through the same stages of growth as the one on the arm. These auto-inoculations occur frequently in places where there are abrasions, caused by eczema or pruritus from other causes, especially on the vulva, hands and face. We call this form, according to Riether, *vaccinosis*. It differs from the vaccine exanthem in its localization, character and time of appearance. The exanthem appears simultaneously over the entire body, and in places which the hand can not reach, vaccinosis only in places with which the hands can come in contact. The exanthem is mostly papular, pock-like formations are rare. Vaccinosis forms typical pustules. The exanthem appears in the fourth period, vaccinosis in the second or, at the latest, the third period. The best prophylaxis against vaccinosis consists in watching the children until the wound is dressed, and a few hours after vaccination washing the skin carefully.

Auto-vaccination may occur in the second period by carrying the contents of an open vesicle to other parts. The new foci resemble secondary vaccinations, but do not become very large because their development is arrested at the beginning of the fourth period. Because of this auto-vaccination, we do not vaccinate children with eczema and lichen urticatus. When vaccination becomes necessary because of danger of smallpox, the child's arm must be carefully watched and not left without a sleeve. It may even become necessary to bandage the hands, or by applying a cuff over the elbow, to prevent flexion of the forearm.

A broken vesicle is less dangerous to the child than to his associates. Most cases of severe vaccine infections arise among children of the same family who have not been vaccinated, or among adults who have been vaccinated a long time previously, by playing with a vaccinated child and thus carrying the material to the eyelids, nose, areas of eczema, etc.

Unvaccinated children should therefore be kept separate from the children at the height of vaccinia.

Complications caused by pathogenic bacteria contained in the lymph are extremely rare. In the earlier days when the arm-to-arm method of vaccination was in vogue it occasionally occurred that syphilis was transferred. After the vaccinia there appeared a regular primary syphilitic lesion at the site of vaccination. This danger, as well as that of transmission of erysipelas, pemphigus, furunculosis, and septic processes, is now avoided by the use of animal lymph. Secondary infection of the pustule by scratching with dirty fingers does, of course, occur, resulting most commonly in suppuration, and causing prolonged duration and a hard infiltration of the sore. Erysipelas may also follow. A diagnosis can only be made when the pustule is broken and after the disappearance of the areola. There reappears a sharply outlined infiltrated redness at the site of vaccination and there is temperature. Many supposed cases of erysipelas are, in reality, only very prominent areolas.

Protracted complications and constitutional changes in a child after vaccination are not scientifically proven. I do, however, believe that the fever period of vaccination is quite favorable to the outbreak of a latent syphilis or tuberculosis, as is the case with tuberculosis after measles. Therefore, it is well to vaccinate during the first year of life, before tubercular infection has taken place.

Few facts in medicine can be so clearly demonstrated as the extermination of smallpox by means of vaccination.

It may be said that vaccination may, perhaps, prevent a subsequent infection with vaccine, but not with variola. Regarding this point, a great number of careful experiments were made at the beginning of the nineteenth century, where secondary inoculation with variola was practiced after vaccination to study its efficacy. The immunity of vaccinated persons against both processes was clearly proved.

The principal objection of those opposed to vaccination, not to speak of the great fear of the transmission of syphilis, is the belief that in spite of vaccination one may be attacked by variola. The gradual recurrence of a marked revaccination effect is analogous to this fact, well known since the early part of the nineteenth century, that just as revaccination (the accelerated reaction) is almost never just like the first vaccination, variola of the vaccinated differs similarly from that of the unvaccinated in its course. It is as a rule abortive, and very rarely fatal. The early hæmorrhagic form which attacks vaccinated robust men is, perhaps, an exception and is, no doubt, analogous to that form of revaccination which, during its rapid course, produces a large areola.

How long does the protection against smallpox last? It is difficult to answer this question accurately, because of the many individual variations. Statistics on this point vary between twelve and twenty years. The protection seems to be of shorter duration among children than that following vaccination of adults. Statistics on successive revacci-

nation somewhat enlighten us. We may assume that those whose revaccination was successful, that is, resulted in a well-developed pustule, would, if infected with variola, have developed a smallpox eruption.

Of 1342 children, whom Heim revaccinated at the age of one to five years, 2 per cent. showed reaction resembling a normal first vaccination. Among 1418 children, between five and ten years of age, the percentage was 5.8. Among children between ten and fifteen years, 9.6. We may conclude, then, that of the first group 2 per cent., of the last as high as 10 per cent., were predisposed to the development of variola.

From a practical point of view, the efficacy of the German law regarding vaccination has been sufficiently demonstrated. It requires vaccination during the first year and revaccination in the eleventh year. Most men are again vaccinated on entering the army. Although we can not with certainty predict that an individual is protected against smallpox, the danger from a case of smallpox is so slight that an extensive spread of an epidemic rarely occurs.

DIPHTHERIA

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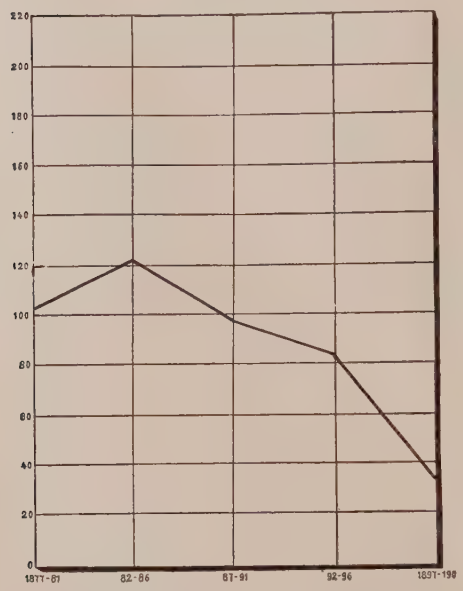
History.—Diphtheria is the term applied since the time of Bretonneau and Trousseau to a disease of the mucous membranes or skin, occurring epidemically and spreading by contagion, and characterized by the formation of a membranous deposit with general symptoms of specific toxæmia. Physicians had long been acquainted with the local manifestations of the disease, such as diphtheria of the pharynx, larynx, skin, etc., but the relationship between these different types of the disease was first recognized by Bretonneau and his pupils, Velpeau and Trousseau (1821–28).

The exciting cause of the scourge, a peculiar bacillus, was first discovered in diphtheritic pseudomembrane by Klebs in the year 1883, while Löffler in 1884 was the first to obtain it in pure culture and to demonstrate its pathogenic action in the lower animals. Although these bacilli could be found in almost every case on the mucous membrane attacked by the diphtheria, and although Löffler succeeded in producing pseudomembranes similar to the diphtheritic deposits by rubbing bacilli into the injured tracheal mucosa of rabbits, the etiologic importance of the bacilli would nevertheless have remained in doubt if Roux and Yersin had not been able to isolate the toxin produced by the Klebs-Löffler bacillus and in experiments on lower animals to produce with it the main symptoms of diphtheria, especially the characteristic paralyses. The discovery of the exciting cause of diphtheria was followed ten years later by the discovery and introduction of a specific treatment for the disease, von Behring's serum therapy. Received at first with scepticism, the use of diphtheria antitoxin has in a few years conquered the whole world. Diphtheria, however, still belongs in the class of dangerous diseases, but physicians can now face its dangers with a certain superior calmness, based on a consciousness of a clear knowledge of practically all the variations of the disease and on the possession of a remedy with a sure action in the majority of cases.

Epidemiology.—Diphtheria is seen in all climates and seasons but is more prevalent in cold countries and the colder months. While in the earlier centuries it apparently always occurred in more or less sharply

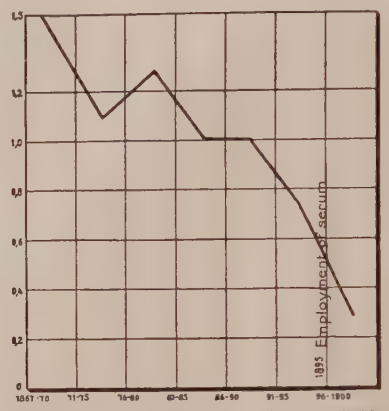
defined epidemics, by the middle of the Nineteenth Century it had become pandemic, owing to the development of commerce with more rapid means of transportation, so that now the disease practically never dies out in large cities. In addition, the epidemics have shown great varia-

Fig. 77.



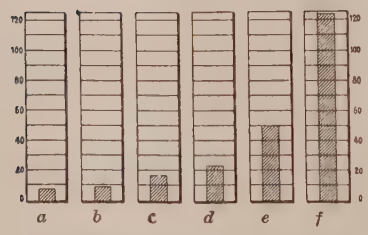
Diphtheria mortality in the German Empire, 1877–1901.

Fig. 79.



Diphtheria mortality in Munich, 1867–1900.

Fig. 78.



Infectious diseases, mortality in Germany, in 1900. *a*, typhoid fever; *b*, scarlet fever; *c*, measles; *d*, whooping-cough; *e*, diphtheria; *f*, tuberculosis.

Fig. 80.

Total mortality of diphtheria in Gratz 1890–1903, in per cent.

tions in intensity, in the course of a single year as well as over longer periods. In the preceding century the mortality from diphtheria in Germany rose steadily until it reached its highest point of 122,000 deaths in 1886 (see Fig. 77 and "Century-curve of Mortality from Diphtheria in Hamburg," Heubner's Text book.) Since then it has fallen with an increasing rate of decline to about 45,000 fatal cases in

1900 (Fig. 78). Marked differences were often shown by the different cities, this variation in each locality being dependent upon the favorable or unfavorable character of the disease, which can change from year to year in any place. Figure 79 shows the diphtheria mortality in Munich, the maximum being passed long before 1886. The chart giving the number of deaths does not show so decidedly the introduction of the antitoxin as does the chart giving the percentage of the fatal cases (see Fig. 80, percentage of fatal cases in Gratz). The approximate proportions of the favorable and severe forms of diphtheria for the last decade in German cities is given in Fig. 81.

Fig. 81.

Localized tonsillar diphtheria
56% of cases mortality 1-2%
Diphtheria gravissima
1% of cases mortality 24%
Descending diphtheria (croup)
33% of cases mortality 17,8 %

Table showing the frequency of the clinical forms of diphtheria and their mortality.

The primary localization of the disease and its character, as well, have changed at different times. We now see the disease beginning almost always in the pharynx, and other initial points are rather rare. In the first half of the preceding century, however, primary diphtheria of the skin and larynx were frequently met with; the Saxony physicians before 1860 were acquainted only with croup and looked upon pharyngeal diphtheria as a great rarity. In former times also, adults were very much more frequently attacked by the disease than is the case to-day. Nowadays, diphtheria is seen, with few exceptions, only in children. The greatest morbidity and mortality occur between the ages of two and five years. The susceptibility of infants shows a great increase after the age of six months. From the school age to adult life the incidence of the disease and its mortality show a steady decline.

ETIOLOGY

THE DIPHTHERIA BACILLUS

The exciting cause of diphtheria is a bacterium belonging to the group of the actinomyces, whose form, growth and virulence show marked changes according to the culture-medium and the age of the culture.

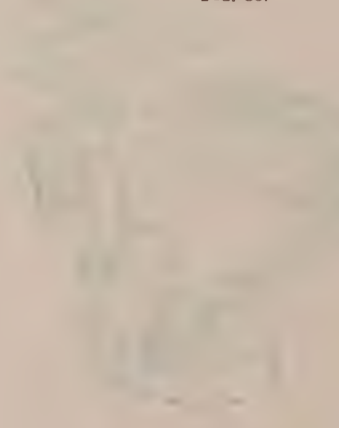
Morphology.—Löffler describes it as a non-motile, straight or slightly curved rod—with an average length of that of the tubercle bacillus but about twice as broad—showing rounded or often swollen ends, and under certain conditions appearing stratified or granular through an irregular absorption of the stain (thickening of the chromatin, appearance of degeneration, involution forms). In a smear preparation,

the rods lie parallel or at angles to each other in groups of various sizes, frequently forming letter-like figures, as V, W, X or Y. In sections of the pseudomembrane they are seen grouped in large or small nests or arranged somewhat like a fish's tail. In addition to the typical

Fig. 82.

Diphtheria bacilli from membrane taken during life. Stained with Löffler's potassium methylene blue solution. Washed in water. From Vierordt's Diagnosis.

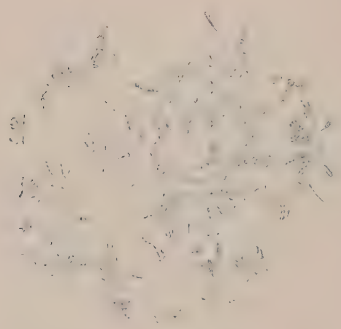
Fig. 83.



Diphtheria bacilli mixed with cocci. From membrane taken during life. From Vierordt's Diagnosis.

Löffler form of the long bacillus, there are frequently seen young, shorter forms which are not granular and are wedge-shaped or cylindrical, and also giant-forms, two or three times as large, with bulbous ends which are always decidedly granular and stratified, so that they are easily mistaken for cocci. Under certain exceptional conditions of growth there are seen thread-like forms which may or may not branch (Abbott and Gildersleeve).

Fig. 84.



Diphtheria bacilli (Löffler) from bouillon culture. Stained with Löffler's methylene blue. Zeiss homog. Immers. $\frac{1}{12}$, Ocular 4. From Vierordt's Diagnosis.

Staining.—The diphtheria bacilli take all the aniline stains readily, and resist Gram's with only a short application of the iodiniodide of potash solution. A good picture is furnished with Löffler's alkaline methylene blue solution (30 c.c. concentrated alcoholic solution of methylene blue, 60 c.c. potassium hydroxide solution, 1 : 10,000) which ought to be made fresh every four to six weeks. When stained with Ziehl's solution or aniline-gentian violet, the bacilli appear more plump through a swelling of the plasma. Double staining is recommended to bring out the Babes-Ernst granulations and especially to differentiate the chromatin from the enveloping substance; Roux uses

dahlia violet and methyl green, Neisser's method being acetic acid-methylene blue, crystal violet and chrysoidin. The value of double staining is discussed in the section on diagnosis.

Growth.—The diphtheria bacillus needs for its growth a culture medium with slightly alkaline reaction. The limits of its growth lie between 19°–42° C. (66°–107° F.), the most favorable temperature being from 33°–37° C. (91°–98.6° F.). It grows most luxuriantly on an albuminous medium, especially blood-serum, which is used as a selective medium; for the bacillus develops on this more rapidly than other bacteria which may accompany it. From eight to twelve hours after inoculation a growth of minute colonies is seen on the surface of the serum looking like ropes of droplets which soon become confluent and in about two days cover the culture medium with a thick white overgrowth, the edges of which are scalloped. In bouillon the effect is first to give an acid reaction and after not less than eight days a return to alkaline. The bacilli grow luxuriantly in milk without curdling it. With the development of an acid reaction in the culture medium, the growth and the formation of toxin (Madsen) lessen. A similar result follows a change of temperature to that above or below the limits mentioned.

The *sensibility of the bacilli* to thermic influences is very varied. Cold, even the action of winter-temperatures for months, is well borne (Abel), but in the opposite direction, death soon follows the action of a temperature of 50° C. (122° F.). The bacilli are just as sensitive also to the action of certain chemicals, especially those used ordinarily in disinfection in the usual strengths:—alcohol, lysol, phenol, tincture of the chloride of iron, chlorine water, corrosive sublimate, cyanide of mercury. Much less powerful are boric acid and permanganate of potash, but peroxide of hydrogen is very useful.

Although the bacilli resist heat and chemicals so feebly, their resistance to drying is in the inverse ratio, especially if they are enclosed in bits of membrane and are not exposed to diffused daylight. Positive cultures have been obtained after weeks and months from toys and books, from furniture, dishes, floors and walls of previously infected dwellings, especially if dark and damp. It is noteworthy that the bacilli are able to endure a temperature of 98° C. (208° F.) for an hour in the dried pseudomembranes (Roux and Yersin).

The diphtheria bacilli have a *pathogenic action on lower animals* only when introduced artificially. If the tracheal mucosa of a rabbit is injured by traumatism and the bacilli injected, the animal dies with symptoms similar to those in membranous croup. At the autopsy a fibrinous, hæmorrhagic exudate is found on the trachea. The mucosa around the site of the inoculation is strongly reddened and covered with a grayish yellow, thick, tenacious pseudomembrane, from which the bacilli can be cultivated. Identical appearances follow if, instead of the

bacilli, a germ-free filtrate of a culture is used for the injection, one being chosen which does not cause death too suddenly (Roux, Roger and Bayeux, Trumpp and Ziegler). Control-animals recover from the traumatism very promptly and the mucosa shows only small red deposits. While the animals in such experiments die from obstruction of the trachea, when the bacilli or the toxin are injected subcutaneously or intraperitoneally the animals die with symptoms of general intoxication and if the course is prolonged, paralyses occur which resemble the post-diphtheritic paralyses in human beings.

The typical findings are fibrinous exudate at the site of injection, inflammation of the serous membranes and hyperæmia of the adrenals. If the bacilli are injected they are found only at the site of inoculation. Death can therefore be the result only of intoxication. *The fact that the pseudomembranes which follow the injection of bacilli are also caused by an injection of the germ-free toxin proves that their development is to be attributed to the action of the poison.*

In the animals which survive the injections there is found an increased resistance to the action of further doses of the toxin, but this acquired immunity to the poison does not prevent the possibility of diphtheria bacilli obtaining a foothold and multiplying on the mucous membranes. *On the ability to transfer from animal to animal and from animal to man this condition of immunity rests Behring's serum therapy.*

Not all of the Löffler bacilli are pathogenic. Their virulence, or the ability of their protoplasm to produce toxin is very different (but not necessarily so) in that bacilli from mild cases are less virulent than those from severe cases. The results of animal experiments and clinical observation often harmonize, but not always. This lack of harmony is probably due to the variations in the living material, and also sometimes to chance in the experimentation. The bacilli cultivated from one case do not all show the same degree of power, as virulent and non-virulent may be found side by side. The latter either show all the characteristics typical of the Löffler bacillus, or vary somewhat in their morphological or cultural peculiarities, which has led Löffler, Hoffmann-Wellenhof, Escherich and others to view them as a special kind of bacilli, the pseudo-diphtheria bacilli. But since it has been possible by a passage through animals, whose resistance has been lowered by non-fatal doses of diphtheria toxin, to change typical pseudodiphtheria bacilli into highly virulent diphtheria bacilli, typical morphologically as well as culturally (Trumpp), they can no longer be considered a distinct species.

This experiment also throws interesting light on the activity of other bacteria which accompany the diphtheria bacilli in the so-called *mixed infections*. The latter are looked upon mainly as secondary processes in which pyogenic cocci and bacteria of putrefaction play the main rôle. We cannot yet grant that they enter into a kind of symbiosis

with the bacilli and thereby increase the virulence of the latter (Roux) but rather that their entrance into the tissues and fluids is made possible by the activity of the diphtheria bacilli, and that the cocci in turn lower the resistance of the organism to the bacilli or their toxin. They can be looked on as sharers in the disease-process only when they are deep in the pseudomembrane or in the submucous tissues, but not if they are only lying on the pseudomembrane, for dozens of species of streptococci and staphylococci are included among the common inhabitants of the mouth and are found, in consequence, also in the superficial layers of the false membrane. When the mixed infection is streptococcal, the symptoms are like those of other septic processes. According to Bernheim, blood-infection is not always necessary, as the process need not advance further than an intoxication, the streptococci remaining in the false membrane while their toxins are absorbed. The result then is a combined action of the toxins of the diphtheria bacilli and streptococci.

In almost all cases which show the clinical course of diphtheria Löffler bacilli are found in the local deposit. As a rule they are found only in the necrotic tissue and exudate, in the lymph-spaces and the regional lymph-nodes. Instances of the bacilli in the blood during life or in the blood and internal organs after death are extremely rare. Some time after the decline of the attack, the bacilli disappear from the pharynx but they may remain for weeks and months capable of multiplying, and in a virulent state, on other mucous membranes, in the nasal passages, on the conjunctiva or the vulva. The bacilli are spread from one person to another by contact with the sick and convalescent and also by articles and food infected by them (milk). It is now fully established that virulent Löffler bacilli can settle on the mucous membranes of healthy persons without causing symptoms of the disease; and so frequently have bacilli which belong beyond doubt to the family of Corynebacterium diphtheriæ been found in the nose and on the conjunctiva of children and adults who, so far as is known, have not been in contact with diphtheria patients, that the diphtheria bacillus may be considered almost ubiquitous. These considerations show us that the mere presence of the bacilli is not sufficient for the development of the disease.

PREDISPOSITION

For the development of diphtheria it seems that much more [than the presence of the diphtheria bacillus] is necessary: (1) that the bacilli have attained a certain degree of virulence; (2) that these bacilli be borne in large numbers to the mucous membranes; (3) that the infected mucous membrane is at the time of infection in a condition which gives a footing to the bacilli and favors their increase, which condition is a not too acid reaction with a loosening or abrasion of the epithelium; (4) that the

infected individual is in a general way receptive, having neither sufficient general resistance nor inherited nor acquired specific immunity, or at least only to an inadequate degree.

A potential predisposition may at times be increased or lessened, or it may first make itself known when the general vitality is lowered by an accidental sickness which in itself is quite insignificant.

Little that is positive is known about the special local predispositions. A lowered predisposition may be reasonably attributed to a mucosa of firm texture, and in infants during the early months of life to the acid reaction of the buccal cavity, especially. An increased tendency may possibly be found among individuals with hypertrophy of the lymphoid structures of the pharynx, which form in the majority of cases the starting point of the local process. In the same way all affections which produce a loosening or inflammation of the pharyngeal mucous membrane, seem to favor the infection.

Numerous investigations point to the existence of an antitoxic state of the blood, not only in convalescents from diphtheria, but also in children, even up to the eleventh year, who, as far as known, have never had diphtheria. The transmission of an immune body in the milk of women convalescent from diphtheria to the infants nursed by them is doubtful (Auden).

In general, a disposition to contract diphtheria is present in relatively few persons, probably because of congenital immunity; at least the figures for the morbidity appear rather low in proportion to the numerous opportunities for infection. The very frequent occurrence of the disease in early childhood can in part be attributed to the fact that children of this age are creeping on the floor and putting their soiled and infected fingers frequently into their mouths (Feer). The immunity of adults in spite of equal chances for infection [members of the same family] is not fully explained.

In the majority of cases, survival of an attack of diphtheria furnishes an immunity for the rest of the individual's life, and yet instances of second and third attacks are not rare (according to Zucker in 9 to 13 per cent. of all cases).

Pathogenesis.—Under the above-mentioned conditions the diphtheria bacillus may act in a specific manner on the human system. It settles on a predisposed mucous membrane, especially the pharynx, and multiplies with rapidity. If the number of the bacilli and the toxin manufactured by them are sufficient, for which a varying length of time of from two to seven days is necessary, probably dependent on the difference in the local predisposition and on the amount and intensity of the infecting virus, then there arise symptoms of a local process followed later by those of a general intoxication.

The next step consists in certain changes in the mucous membranes.

The poisonous metabolic products of the bacilli set up coagulation necrosis of the epithelium, which furnishes a still more favorable culture medium for the germs of the disease. At the same time the poisons diffusing through the epithelium set up a decided inflammation of the limiting layers of the mucosa. The blood vessels in the region become dilated and engorged and following the injury to their walls they pour out rapidly and richly an exudate of serum and fibrinogenous substance. The fibrin ferment set free by the death of the tissue-cells causes a coagulation of this exudate pressing into the necrotic epithelial layers, and through constant repetition of the process a pseudomembrane is formed.

So long as only the superficial blood vessels are exposed to the action of the poison, the exudative process is limited to the epithelial layer of the mucous membrane. The false membrane lies *on the mucosa* and can be easily removed. But when the vessels of the submucosa are affected there then follows fibrinous exudation in the subepithelial layers also, and the false membrane is then formed *intimate with the mucous membrane,* so that it can be removed only with difficulty, its removal causing bleeding (croupous or diphtheritic process in the anatomical sense).

The compression of the vessels by the fibrinous exudate and the impeded circulation cause in addition a *necrosis* of the affected tissues so that after the spontaneous removal of the false membrane deep ulcers are left behind. If gangrenous processes set in, changing the mucous membrane into an offensive, dirty, liquefying mass or into a firmer blackish crust, there may then occur widespread destruction of the mucous membrane going on even to destruction of the underlying cartilages. Mention must also be made of the fact that degenerative processes in the blood vessels occur not only at the site of the local processes but also in situations far removed, points of election being the lung, pleura and adrenals.

The *lymph-nodes* near the local manifestations are always affected, and even the remote lymph-nodes, though in a lesser degree. They are swollen and, in severe cases, inflamed; in gangrenous processes œdematous infiltration also occurs in the periglandular connective tissue.

Sooner or later, following these changes there develop more or less severe general symptoms, which can only be attributed to the absorption into the circulation of the toxins formed at the site of invasion, for the diphtheria bacilli, because of their demand for oxygen, multiply only on the superficial layers of the mucosa, especially of the respiratory tract (preference for cylindrical epithelium), hardly ever penetrating into the fluids and internal organs; when this exceptionally occurs, they very quickly die out. A febrile disturbance follows, and symptoms of degeneration appear, affecting especially the heart, the parenchymatous organs and the peripheral nerves.

The clinical picture produced by the diphtheria bacilli and the germs ordinarily aiding them, shows certain fundamental differences: (1) according to the location of the invading germs; (2) according to the behavior of the attacked mucosa toward the invasion; and (3) according to the quantity and quality of the toxin, on the one hand, and on the susceptibility of the patient, on the other.

The onset and course of the disease may be violent or gradual, and sometimes the local, in others, the general, symptoms predominate.

The mucous membrane reacts to the bacillary irritation often with only slight superficial inflammatory products, in other cases with a penetrating inflammation and profuse fibrinous exudation. This may happen in the same individual, the mucosa in different places showing a varying reaction to the same infection.

The general symptoms of toxæmia may be limited to a moderate fever of brief duration with a transient albuminuria, or it may comprise severest disturbances of the general well-being, with marked albuminuria, affection of the myocardium and paralyses. Local and general predisposition usually go parallel to each other, but this is by no means always the case (Escherich). Thus, severe toxæmia may accompany very slight local deposits, and, on the other hand, the general condition may be practically undisturbed with extensive membrane-formation.

The local process, as well as the general intoxication, can bring about a fatal termination. The local process does so when it is situated in the air-passages, with an inflammation of such high degree that the swelling of the soft parts and the pseudomembranous formation prevent the entrance of air. The general toxæmia results in death when it causes irreparable injury to the vital organs, especially the heart. Finally, death may be caused by infection.

Natural recovery follows the action of non-specific protective bodies, already present, the alexins of the blood, as well as the specific reaction of the organism by which the effect of the diphtheria toxin is in part neutralized. The loosening of the pseudomembrane appears to be brought about in a special way by the entrance of staphylococci into the meshes of the fibrin-network, through which they are scattered extensively. Their metabolic products, in a chemotactic way, bring out great numbers of leucocytes to act as phagocytes; these, by their death, favor the destruction and removal of the membrane. Then the fibrin turned to pus or fat is thrown off and expectorated. In the larynx and trachea the deposit is more quickly removed because it is lifted up by the increased secretion of the mucous glands of the membrana propria, and so is loosened in its whole extent. The healing of the ulceration, left after the false membrane has been shed (rare in the larynx and trachea), is brought about by the proliferation of the intact epithelium in the vicinity, which gradually grows over the gap. Very deep diphtheritic

ulcers are followed by permanent loss of substance with scar-formation (healing only by the activity of the subepithelial connective tissue).

ANATOMY

Mucous Membrane.—The mucous membrane affected by diphtheria is swollen, œdematous, strongly injected, often hæmorrhagic, while the pseudomembranes, which vary in extent and in the tenacity with which they adhere to the underlying tissues, show all variations in color from black to white. They are granular, crumbling and soft, or firm, tough and elastic. On section the thin membranes are merely a cellular fibrinous infiltration of the superficial layer of epithelium. In the thick membranes different layers are seen. At the top is a layer of granular detritus in which are found diphtheria bacilli and the saprophytes ordinarily present on the mucosa. Below this is a layer of fibrin with very close filaments containing only diphtheria bacilli and remains of the epithelium which can scarcely be recognized. Next comes a network of fibrin enclosing leucocytes and more or less altered epithelial cells, the filaments becoming further apart towards the mucosa. In "croup" only the superficial layer of epithelium is necrotic, the layer of fibrin with leucocytes sprinkled through it is sharply outlined with its lamellated structure against the stratum proprium. In "diphtheria" the membrane and necrosis extend to the submucosa, fibrin-formation is seen in the follicles of the glands and in the lymph-spaces, in the limiting connective tissue; in the swollen lymph-nodes of the neighborhood and here and there in the blood vessels. At the boundary of the necrotic tissue lies a dense wall of leucocytes (see Plates 22 and 23).

The *lymph-nodes* are swollen, hyperæmic, hæmorrhagic and show diffuse or circumscribed necrosis on section. At times the periglandular tissue is infiltrated. Microscopically there are not rarely found groups looking like miliary tubercles but without caseation or giant-cells. The blood vessels of the lymph-nodes may be occluded with thrombi.

The *lungs* are almost always affected. They may be involved in every part from the bronchial mucous membrane to the pleura. The changes may be simply those of catarrh or more frequently bronchopneumonia with vicarious emphysema. The pneumonia may follow an extension of the catarrhal process, or it may have its starting-point in the formation of infarcts in the blood vessels. Fibrinous, hæmorrhagic or serous exudates in the pleural cavity are of frequent occurrence. Sometimes latent tuberculosis of the lymph-nodes becomes lighted up as a sequel. In addition to pneumococci and streptococci, diphtheria bacilli are also found in the lesions.

As a rule the *heart* shows hardly any perceptible changes macroscopically. It is in diastole and the cavities are filled with firm, fibrinous clots. The heart-muscle is pale, grayish brown and on section,

whitish, somewhat œdematous and brittle. In almost every case the microscope shows decided changes in the myocardium. In rapidly fatal cases there is only decided fatty degeneration. When the cases run a longer course the changes are more severe, consisting of disappearance of the transverse striations, massing together of fat granules (in high degree only when severe anæmia has existed), vacuole formation, with fragmentation of the muscle bundles. In 18 cases of postdiphtheritic heart-paralyses Eppinger found destruction of the muscle fibres resulting from a solution of the cell substance, myolysis, with frequent blocking of the attendant muscle-capillaries by destroyed blood corpuscles. The changes most frequently found are those affecting the interstitial tissue with or without involvement of the parenchyma at the same time, consisting of œdema with an aggregation of lymphocytes and fibroblasts. As a result of degeneration of the heart-muscle and connective tissue overgrowth, fibrous myocarditis may develop. In the endocardium primary necrosis is not rare with thrombus-formation following. In the vessels of the heart, as in the other organs proliferation of the intima sets in (see Plate 23).

Disturbances of the *kidneys* from the simplest to the severest forms are found in all cases. The kidneys are usually somewhat enlarged, pale, with the cortex thickened, the medullary substance showing reddish streaks, and the organ as a whole firm, tough, glistening and moist. Microscopically about two-thirds of the cases show exclusively or at least principally a degeneration of the epithelium, especially of the convoluted tubules and the descending Henle's loops. For the most part the cells are non-granular, swollen and containing fat-droplets, and in many places they are so completely destroyed that only a structureless mass remains (Diphtheritic parenchymatous nephritis, Plate 23). Numerous hyalin casts are seen in the collecting tubules (Heubner). Interstitial changes, massing of cells in the blood vessels and infiltration of the connective tissue as well as the very rare involvement of the glomeruli, are found almost solely in older children after a protracted course of the disease. Exceptionally, hæmorrhage into the tubules and chronic processes in the form of atrophy are found (Councilman, Mallory and Pearce).

The *liver* is large, glistening, blood-red, firm and moist, with the acini visible, and on microscopic examination shows decided parenchymatous degeneration.

The *spleen* shows nothing macroscopically except swelling of the follicles. Microscopically there are seen hyalin degeneration of the arteries and foci of epithelioid cells.

The *peripheral nerves* show in many cases fatty degeneration of the medullary sheath with swelling and disappearance of the axis-cylinder (degeneration starting from the medullary sheath) and an overgrowth of connective tissue.

Types of the Disease.—According to the location, distinction is made between diphtheria of the pharynx, nose, larynx, vulva, conjunctiva and of the skin, or wound-diphtheria. The most frequent variety is diphtheria of the pharynx, which usually appears in a localized, favorable form, but it may show a progressive character with more or less toxic symptoms, or it may assume a highly malignant gangrenous type. Ordinarily a case shows the triad of symptoms, necrosis of the mucous membrane, fibrinous exudation and presence of the Löffler bacilli. Transitional forms are often seen.

1. PHARYNGEAL DIPHTHERIA

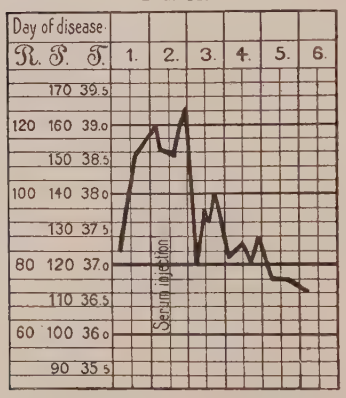
(*a*) LOCALIZED PHARYNGEAL DIPHTHERIA

Onset.—At the start subjective symptoms of discomfort are so slight that it is usually difficult to fix a definite onset for the disease. The children feel somewhat tired, they are disinclined to eat and to play, they are sleepy, the voice is rather hoarse and slightly nasal from moderate occlusion of the nostrils. The child breathes through the mouth and the respirations are visibly accelerated. Occasionally the onset is very sudden, with chill, high fever and headache. An unpleasant odor to the breath and elevation of temperature are usually the first symptoms that bring the child to the physician and although the child has not seemed sick enough to be put to bed it looks pale and tired. The cervical lymph-nodes, especially those at the angle of the jaw and sometimes also the submaxillary nodes, are swollen on one or both sides, being hard and somewhat movable. An irritating discharge flows from the nostrils. The pulse and respiration are accelerated, and the first sound of the heart is often rather impure. The temperature is usually between 38° and 39° C. (100.4° to 102.5° F.) and is rarely higher. Pain in the neck and discomfort on swallowing are sometimes present early. On inspection of the mouth and pharynx only slight evidences of inflammation are seen. The tongue is dry and moderately coated, the pharyngeal mucous membrane is a little reddened and glistening with increased secretion, the pillars and tonsils of one side, rarely both, are prominent. On the tonsil, less frequently on a swelling to one side of the posterior pharyngeal wall is seen a small, slimy-looking deposit which, after wiping away the mucus, is found to be a pseudomembrane adherent to the mucosa and without sharply defined edges (Plate 21). In a still earlier stage the appearance is that of a web-like etching on the mucous membrane. It can usually be loosened without injuring the underlying structures and if it is rubbed between two cover-slips, the firmness of its structure can be appreciated. On staining the preparation, fibrin is found with Löffler bacilli aggregated in clumps, in company with the saprophytes of the oral cavity. The further course of the case depends on whether or not the specific treatment is adopted.

If the antitoxin is injected immediately, the spread of the membrane ceases, or during the next twenty-four hours it extends over only the immediate surroundings; new deposits of fibrin, ordinarily only small ones, may appear during this time on various parts of the pharyngeal or oral mucosa as a result of the action of the germs before the administration of the antitoxin. With a rapid fall of the temperature and pulse to the normal, the pseudomembranes undergo liquefaction, they become sharply circumscribed and are either thrown off in flakes or melt away more slowly, disappearing entirely by the end of the third day. Eight days after the onset of the first symptoms the children feel so completely recovered that it is almost impossible to keep them in bed.

Without the gracious help of the antitoxin the course of the disease is usually very much more protracted. The membrane appears on symmetrical parts or spreads by continuity until it may finally cover like a velvet skin both sides of the fauces, the uvula and even small spots on the posterior pharyngeal wall. It then remains stationary for five or six days (Plates 21 and 22). Sometimes the nasal passages are also affected but here the diphtheria is seldom so intense as to lead to the formation of false membrane. There are catarrhal changes with a profuse discharge, sometimes thin, sometimes mucopurulent or of pure pus, and the voice has a decided nasal character. One nostril is more obstructed, as a rule, than the other. With the spread of the local condition the general condition becomes worse (but to this there are exceptions) with pain on swallowing, tenderness on palpation of the lymph-nodes, with increased depression and total anorexia. The pulse is accelerated in proportion to the fever which falls more slowly than when the antitoxin is used. Moderate albuminuria is found in some cases. The entire course rarely lasts longer than a week, but convalescence is protracted. The prognosis without antitoxin is always doubtful, for even in apparently mild cases the local condition may suddenly spread to the larynx, or severe toxæmia or secondary infections may occur. Postdiphtheritic paralysis is also met with at times, even when the case has not been one of great severity.

FIG. 85.

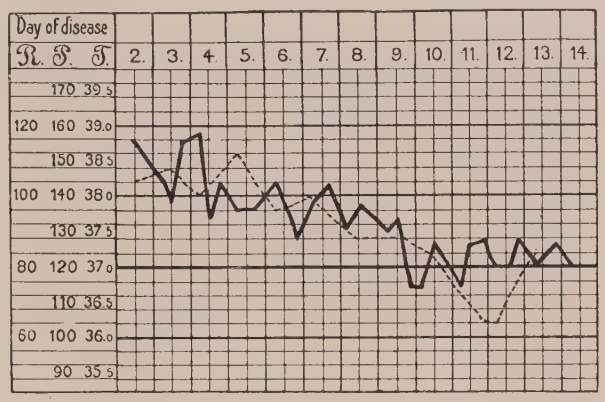


Moderately severe diphtheria localized in the pharynx with typical influence of the serum.

In addition to this which is the ordinary form of localized diphtheria, *rudimentary forms* are seen from time to time presenting such slight symptoms clinically that the diagnosis is suggested by the simultaneous occurrence of typical diphtheria in other members of the household and the suspicions become confirmed by bacteriological study.

In some of these cases there is a slight pharyngeal catarrh with a mottled clouding of the tonsillar epithelium, the merest suspicion of a membrane. There is very moderate fever and complete recovery in a few days. In other cases the exudate remains limited to the crypts of the tonsils and the appearance and course of the disease show great similarity to ordinary follicular tonsillitis. A further discussion of these and other forms resembling tonsillitis and stomatitis will be found in the section on differential diagnosis.

FIG. 86.



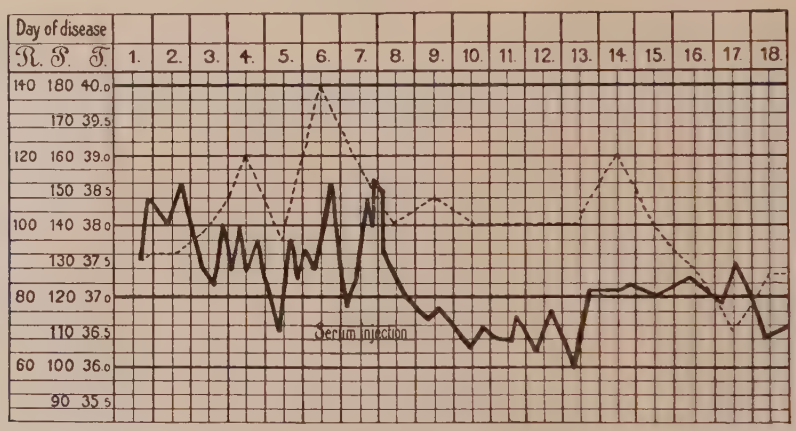
Localized pharyngeal diphtheria in pre-antitoxin days.

(*b*) PROGRESSIVE PHARYNGEAL DIPHTHERIA

The onset of this form may, like the preceding, be insidious and run a rather mild course with moderately severe symptoms of general toxæmia, as long as the affection of the larynx is not so great as to offer considerable obstruction to the entrance of air. In the majority of cases, however, the disease sets in abruptly and with severe symptoms, even with convulsions in very young children. The children suddenly feel very sick, sometimes they are chilly, there is severe headache with general pains in the body, the appetite is gone, they may feel nauseated and they sit around listless and dull with flushed, swollen features. When put to bed they lie rather apathetic with a temperature of 39°–40° C. (102°–104° F.), and the pulse is proportionately accelerated to 140 to 160. The submaxillary lymph-nodes are tender and swollen to the size of a hazel-nut while those at the angle of the jaw are as large as a walnut and sometimes the surrounding region is prominent with a boggy swelling due to œdema of the subcutaneous connective tissue. The tongue is moist and slightly coated and there is a profuse secretion of tenacious glistening mucus in the mouth and pharynx. The mucous membrane of the mouth is bright red while that of the isthmus and of the posterior pharyngeal wall is dark or streaked with red. The faucial pillars, the tonsils, the uvula and the lateral roots of the posterior pharyngeal wall are swollen, usually more on one side. On one or both tonsils there is a uniform, mucous exudate, firmly seated, rarely appearing only as isolated yellowish fibrinous streaks or spots. By the end of the first or the beginning of the second day of the disease the

children complain of burning and choking in the throat and of sharp pains on swallowing, especially when the mouth is empty. Both tonsils and ultimately the uvula and parts of the posterior pharyngeal wall are now seen to be covered with a grayish white membrane, often mottled and either smooth or lumpy in appearance. In the course of the next two or three days the *membrane spreads*, finally covering the whole pharynx, the anterior and posterior pillars of the fauces and advancing up into the posterior nares. The fever and the severe disturbances of the general system continue or even increase in force. The *odor* from the mouth becomes unpleasant, sweetish, even fetid. The sense of fulness in the throat causes dyspnœa. The *voice* becomes thick and, through fixation of the faucial pillars and occlusion of the nasopharyngeal space, decidedly nasal. Secretion is so greatly increased in the nasal passages

Fig. 87.



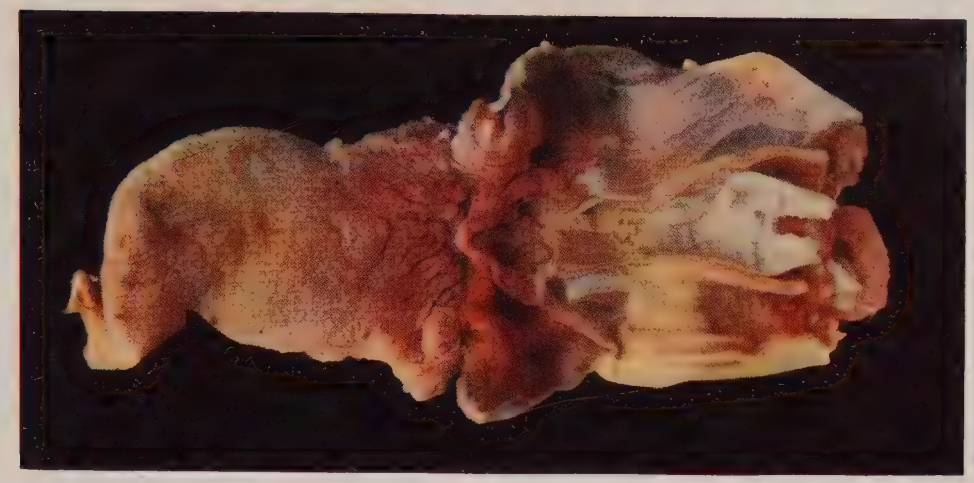
Progressive diphtheria terminating in recovery. Antitoxin, intubation, secondary tracheotomy.

as to occlude them, so that the child breathes with the mouth open. *Otitis* is not a rare complication.

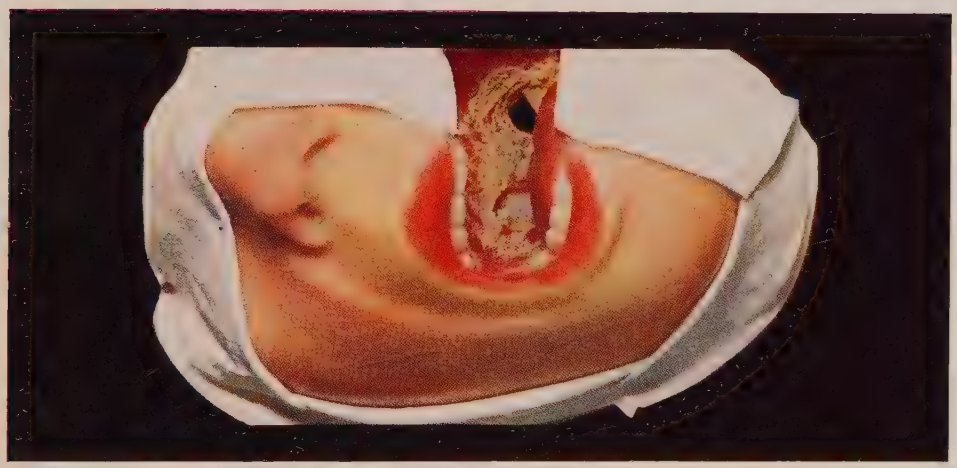
The *kidneys* are affected in almost every case. After about the third day an abundant sediment is found consisting of many small epithelial cells, cylindroids and epithelial casts; from the first to the third weeks of the disease there is albuminuria, varying in amount but never being very great (Heubner).

As a rule the bowels are sluggish even far into convalescence. Examination of the *blood* shows a very decided leucocytosis (L. G. Simon). In cases tending to recovery the proportion of the lymphocytes is increased; in severe cases myelocytes are found (Engel). When antitoxin is injected, the advance of the process is checked in the great majority of cases. The fever falls rapidly and the temperature becomes normal or even subnormal, often within a day. At the same time the pulse-rate falls to its normal, or frequently below, the pulse becoming small and not rarely arrhythmical. The local lesions disappear. The

PLATE 21.



c. Diphtheria of larynx and trachea.



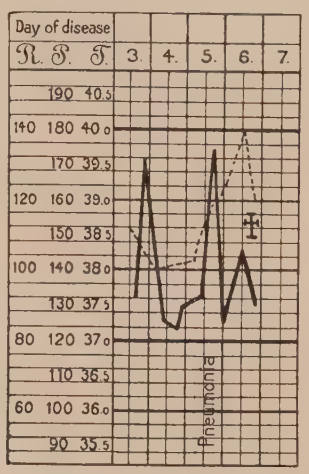
b. Diphtheria of throat, advanced stage.

a. Diphtheria of throat, early stage.

general strength is increased; but the convalescence is nevertheless prolonged by anæmia and general weakness. Not rarely postdiphtheritic paralyses appear, with secondary infections, especially bronchitis and pneumonia, and in many cases there is the threatening danger of an acute cardiac failure, which may also appear very unexpectedly in the acute stage.

If the antitoxin is not given or if its use is delayed until late, the local process may spread by continuity or it may leap to different spots, advancing to the anterior nares, to the larynx and trachea, while in rarer cases the mouth-cavity may show the false membrane. Following these severe local changes, which may sometimes directly threaten life, symptoms of general intoxication set in: rapidly developing general weakness, lowering of force of the heart-beat, evidenced by an ominous pallor of the skin and cyanosis of the mucous membranes; coolness of the extremities due to the poor quality of the blood-stream; right sided or general dilatation of the heart with an impure first sound at the mitral orifice; a small, arrhythmic pulse, becoming slower, finally thread-like and imperceptible. Death occurs toward the end of the second week with collapse, or later than this with uræmia or dropsy.

FIG. 88.



Progressive diphtheria with fatal result. Serum treatment, tracheotomy.

EXTENSION TO THE MOUTH-CAVITY

With the extension to the mouth-cavity there appear on the hard palate, the gums and the lips (Plate 22), rarely also on the buccal mucosa, thin, milk-white deposits which are at first isolated, some of them later coalescing; these false membranes thicken and become grayish green crusts some of which are superficial while others are more deep-seated and can be removed with difficulty and not without bleeding and loss of substance. In very rare instances the whole oral cavity is found lined by pseudomembrane. In all these cases there is increased flow of saliva with an offensive odor to the breath. The regional lymph-nodes are enlarged and infiltrated.

EXTENSION TO THE NASAL PASSAGES, EUSTACHIAN TUBE AND MIDDLE EAR

The false membrane of a pharyngeal diphtheria spreads to the nasal passages by advancing along the lateral wall of the pharynx or else by coming down the front and up the posterior surface of the soft palate, more rarely by a continuous advance from the posterior pharyn-

geal wall up along the base of the skull. High fever develops, and a sense of pressure with obstruction of the nasal passages. Excessive secretion at first serous, later bloody and containing particles of membrane, finally purulent, flows constantly from the nostrils over the lips; it may also be seen in the pharynx, coming down from the posterior nares. The skin of the upper lip and around the nostrils is red, swollen, excoriated and covered with bloody crusts, which may disclose a thin membrane as they fall off. The necessary breathing through the mouth makes the tongue and lips dry and fissured. The voice is thick and palatal. On rhinoscopic examination the mucous membrane is seen to be very red and swollen and on the septum and turbinates there are grayish white deposits, isolated or presenting a frost-like appearance. As a result of the confluence of these spots or by spreading at the periphery the membrane enlarges and may ultimately form a thick, fat-looking layer covering the whole mucosa of the upper air-passages even in its deepest folds, filling up completely the pars posterior (the pars anterior is rarely attacked alone or to any extent). The course of retrogression and healing occur as in pharyngeal diphtheria and take about the same length of time. Deep ulceration may result in cicatricial closures, especially synechia of the septum with the turbinates, closure of the mouths of the Eustachian tubes, partial adhesions of the soft palate with the posterior pharyngeal wall (W. Anton). Sometimes the disease subsides to a chronic form, running for several months and affecting by preference the anterior part of the nasal passages (Concetti, Monti).

Involvement of the nasal passages is not always a grave complication of advancing pharyngeal diphtheria. Sometimes, however, the nose becomes the starting-point of a gangrenous diphtheria. Swelling and œdema of the nose occur with marked pallor and a characteristic shining appearance of the overlying skin (Oertel), involving frequently the cheeks and eyelids. The nasal secretion becomes offensive and of bad odor, while the particles of membrane in it are of a blackish hue and fetid, and profuse epistaxis may occur.

In about three-fifths of all cases the *organs of hearing* become affected. In the mildest form the pharyngeal mouth of the Eustachian tube is closed. The tympanic membrane is strongly retracted and subjective sensations of hearing arise. In other cases the inflammation and fibrinous exudate extend exceptionally through the tube even into the tympanic cavity and mastoid cells (Wendt, Habermann).

Diphtheritic otitis, which may begin very insidiously, is extremely painful. It is accompanied often by violent headache or even disturbance of consciousness, and it causes in the majority of cases large perforations which go on to rapid destruction of the tympanic membrane. Examination with the speculum shows in the beginning only a serous infiltration of the drumhead, obliteration of the outlines of the hammer;

later, after perforation, firmly seated diphtheritic false membranes are seen deep in the external canal or in the tympanic cavity.

The discharge is at first scanty and seropurulent, but after separation of the membranes it becomes copious, fetid and discolored or tinged with blood. The course of such a middle ear suppuration is almost always tedious and frequently injurious through the great disturbances which follow the destruction of the ligaments of the ossicles, through caries and necrosis and the extension of suppuration to the labyrinth. Deafness of high degree often persists and occasionally total loss of hearing (W. Anton) results.

In a way similar to the involvement of the Eustachian tube, the process may spread to the lachrymal canal and even to the conjunctiva (see conjunctival diphtheria).

EXTENSION TO THE RESPIRATORY ORGANS

Extension of pharyngeal diphtheria to the larynx and trachea is somewhat less frequent (one-fourth to one-third of all cases) than to the nasal cavities, although different epidemics may show great variations. Occasionally a continuous membrane is seen extending from the pharynx to the glottis; but as a rule, the larynx becomes involved suddenly on the fourth or fifth day. The primary deposit in the pharynx may not increase, on the contrary it may have begun to lessen, when sudden and unexpected symptoms of croup develop. The onset may be stormy with high fever, prostration, decided swelling of the lymph-nodes, and albuminuria, or it may be more gradual, with moderate irregular fever and less disturbance of the general condition.

The first symptoms are tickling or pains in the neck, a characteristic weakening of the voice, a short, rather brassy cough and a more prolonged character to the breathing. Decided hoarseness develops rapidly, the cough becomes hollow and barking and the breathing is slower, more labored and noisier.

A laryngoscopic examination shows that the symptoms are mainly the result of a swelling and congestion of the mucous membrane, and also partly due to the beginning of fibrinous exudation.

As the case progresses, respiration becomes so embarrassed that the patient is anxious, as shown by the attitude and expression. Voice and cough become almost completely silent. Inspiration and expiration are noisy, lengthened (especially expiration) and extremely labored. The increasing air-hunger brings into play all the voluntary accessory muscles of respiration, so that the thorax is elevated and finally is almost constantly held in the position of inspiration. The number of respirations is somewhat increased to twenty-eight or thirty to the minute. Nevertheless, the volume of air entering the lungs gradually becomes insufficient to counterbalance the external atmospheric pressure and the

parts surrounding the thorax begin to sink in more and more with each inspiration, the suprasternal notch, the supraclavicular fossæ, the epigastrium and in rachitic children the lower ribs. The larynx is drawn down with inspiration.

Although the amount of air entering with each inspiration is so small, yet it suffices, owing to the incomplete expiration, to distend the lungs gradually and to bring about a permanent position of inspiration, so that the lower border of the lungs is depressed. The condition of the patient begins to be wretched, the air-hunger causes excitement, which becomes greatly increased when the respiration is temporarily completely interrupted by loose particles of membrane or mucus. These attacks of asphyxia usually last for only a fraction of a minute, during which the child tosses about in anxiety, the features become cyanosed, the staring eyes seem to start out of the head, beads of cold perspiration come out on the forehead, from time to time the crowing inspiration can be heard at a distance—and death follows unless the obstruction is coughed up, frequently in the form of a more or less complete fibrinous cast of the windpipe (Fig. 89 shows such a cast which extended even to the bronchi of the third division). After the attack the child is exhausted and lies bathed in perspiration; the breathing is better but not easy. Renewed formation and exfoliation of the membrane may cause the attacks to be repeated after six or eight hours.

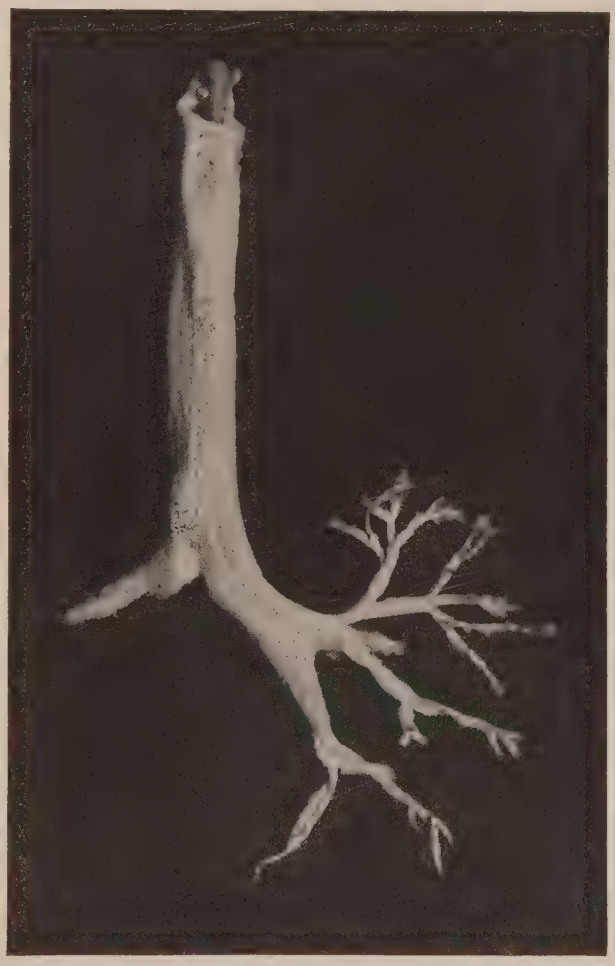
Laryngoscopic examination in the stage of stenosis is exceedingly difficult and one should hesitate to do it. If feasible, it shows a spread of the fibrinous exudate with islands of deposit, some of them confluent, in the interarytenoid space and the subglottic region; or, in extreme cases, a single, uniform whitish yellow (macaroni-like) membrane, extending from the posterior surface of the epiglottis over the false and true vocal cords and on down deep into the trachea. The rima glottidis looks like a narrow, immovable cleft, whose range of excursion is limited particularly by the drawing together of the arytenoid cartilages by fibrinous bands which prevent any movement of abduction (Piniazek) (Plate 21).

All of these symptoms may develop in twelve to twenty-four hours, or it may take several days. If there is no spontaneous disappearance of the threatening symptoms, or if operative interference is not resorted to, the symptoms of carbon dioxide poisoning come on, and the stage of asphyxia is entered (von Rauchfuss).

The patient grows weaker and the activity of the accessory muscles of respiration lessens. The restlessness is followed by an ominous calm. The breathing becomes accelerated, more superficial and the dyspnœa seems to lessen, but the deathly pallor of the skin has a cyanotic tint. The features are drawn, the nose is pinched and prominent and the forehead is covered with a cold sweat. The extremities grow cool. The

pulse may have the paradoxus type, it is rapid, thready and finally not countable. The patient falls into a dreamy doze from which he is roused time and again by the asphyxia, starting up with an expression of great anxiety. From time to time more severe attacks of dyspnœa set in, without, however, causing a marked reaction. This condition persists or tracheal rattle comes on, and life ebbs away slowly after a more or less protracted agonal period, with advancing paralysis of the centres of respiration and circulation.

FIG. 89.



Fibrinous exudate in the larynx, trachea and bronchial tree extending to bronchi of the third degree. Dorsal view, showing the folds of the membrane smoothed out.

The **course** is not so severe in all cases. Some patients have only aphonia and moderate dyspnœa, but these may persist for weeks or exceptionally for months. Even the severe cases may recover (about one-sixth) from the stage of stenosis, by an increase in the mucous secretion tending to dislodge the membrane. Like the local symptoms, the symptoms of specific general intoxication also show great variations. In the advanced stage of the disease it is difficult to separate the action of the diphtheria-toxin from that of the carbon dioxide intoxication.

The successful *outcome of operative interference* depends first on how far the local process has advanced in the air-passages; and next, on the degree of general intoxication, especially on the extent to which the heart is capable of doing its work,—this influencing in no small degree the next important element, the disposition of the deeper air-passages to a primary diphtheritic infection or to a secondary infection with

pneumobacteria (Heubner). If the bronchial tree is already involved at the time of operation, unless the fibrinous exudate becomes melted away by prompt administration of the antitoxin, the outlook for recovery is very dark and the operation is not followed by improvement in oxygenation, the expectoration through the tracheal cannula is weak, respiration remains superficial and rapid, cyanosis and depression increase and death follows in a few hours or days. If the process has been limited to the larynx and trachea, the symptoms of carbonic acid intoxication disappear after the operation and there remain only the effects of the toxin. The outcome is then practically dependent on the time of administration of the antitoxin.

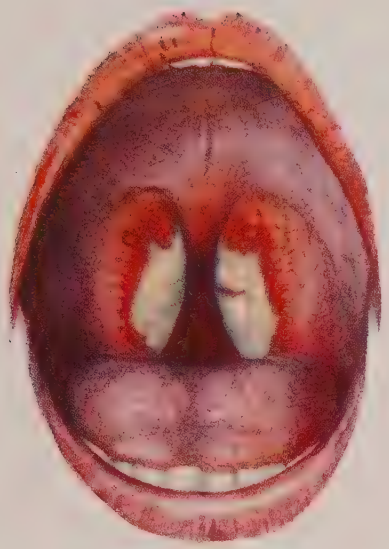
Sometimes, in about half of the cases not treated with antitoxin, after the temporary success of the operation and even with a falling temperature, there comes a turn for the worse due to a descent of the fibrinous inflammation to the bronchial tree, involving in some cases the smallest bronchi. Its onset is marked by an elevation of temperature. Respiration becomes more superficial and accelerated, forty to eighty to the minute. Inspiratory recession is seen at times. The breath-sounds over the lower lobes are weak or inaudible, over the upper lobes they are whistling, sibilant, coarse and accompanied by occasional râles. The further the process advances, the greater is the area of the lung shut off from respiration, increasing by so much the more the carbon dioxide poisoning to which the patient ordinarily succumbs in a day or two.

Far more frequently the fibrinous process stops at the bifurcation of the trachea and the bronchial tree is subject only to catarrhal inflammatory processes, bronchitis, capillary bronchitis, lobular and pseudo-lobar pneumonia. These are caused either by a diphtheritic infection, with the bacilli demonstrable in the affected parts, or by a secondary, non-specific infection with pneumobacteria or the pyogenic cocci. These latter infections are rendered possible through the resistance of the organism being lowered by the general weakness and the diphtheritic toxæmia, and are favored by the lessened expectoration with stasis of the mucus.

As in fibrinous bronchitis, these processes are accompanied by increased fever which continues rather high and with only slight remissions throughout the duration of the illness. The breathing again becomes superficial and accelerated and, like the cough, is painful. Dyspnœa and carbon dioxide poisoning are marked in the severe cases, like descending croup. Auscultation and percussion give no special signs. After a preliminary œdema of the lungs, death follows in collapse, or else there is a protracted course lasting long after the primary diphtheritic infection is overcome.

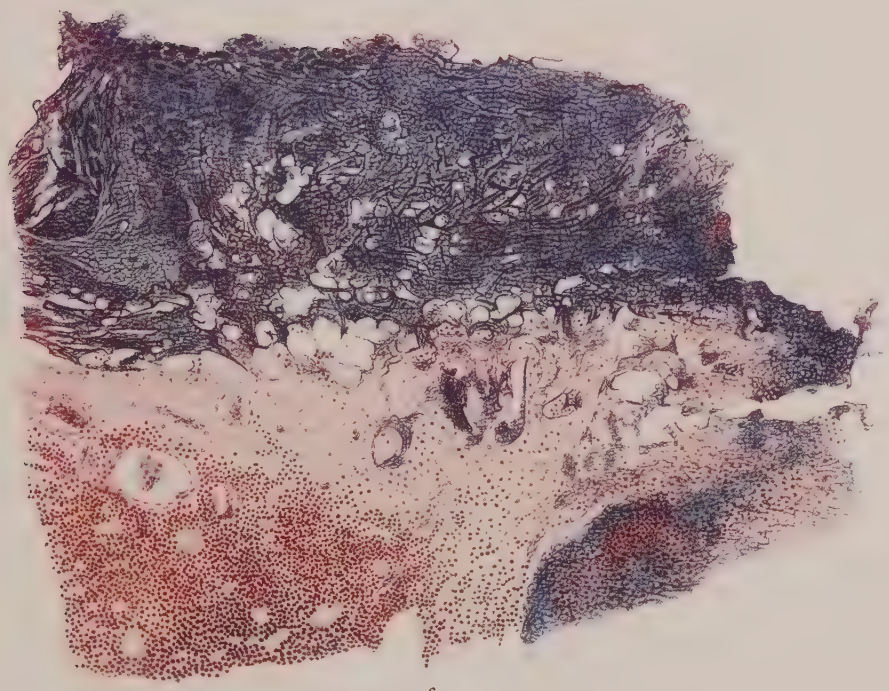
Sometimes serous or purulent pleurisy may arise to complicate the

PLATE 22.



a

b



c

a. Diphtheria of tonsils.

b. Diphtheria of the lips.

c. Diphtheria of the uvula. The epithelium is for the most part necrotic, the cell-nuclei swollen, and the cell-borders no longer recognized. The vessels are enlarged and partly filled with fibrin.

conditions. In other cases the diphtheritic infection produces a dark, hæmorrhagic, infarct-like infiltration of the lung. In such cases there are found small, circumscribed areas of dulness over which bronchial breathing and scattered râles are heard. If the lung parenchyma becomes broken down, cavernous breathing and bubbling râles are heard, followed by septic fever, a putrid odor to the breath, and death. Another possible affection of the lung, which is also accompanied by very high fever and symptoms of widespread pulmonary involvement, is caused by the aspiration of foreign bodies such as particles of food. This is seen especially in operative cases and has as sequels abscess, gangrene or empyema.

(*c*) MALIGNANT PHARYNGEAL DIPHTHERIA, DIPHTHERIA GRAVISSMA

The underlying cause of this most severe form of diphtheria is either an extraordinary virulence of the bacilli (with the combined action of allied streptococci or putrefactive bacteria) or a high degree of individual susceptibility.

It rarely appears in children under four years of age, and its frequency varies greatly according to the type of the epidemic, the average being from ten to eleven per cent. of all cases. It is characterized by widespread and deep-seated lesions of the mucous membrane often with putrefactive processes, localized in many places (pharynx, nose, mouth), and with very severe toxic symptoms. It may be secondary to a localized or progressive diphtheria, or it may be primary from the start.

In the former instance its onset is more insidious, the temperature is hardly raised, while the threatened danger makes itself manifest first in a rapid and profound anæmia and decided lymph-node enlargement.

The *primary form* sets in with incredible swiftness and violence. So sudden is it that in a brief space of time all resistance is battered down. The first symptoms are fever and vomiting with tenderness on pressure in the epigastrium. The patients are greatly excited, sleepless, occasionally slightly delirious, and they soon become prostrated and apathetic. Small red spots appear on the cool, dusky skin. The features are bloated or very sharply drawn and the eyes are dull. From the open mouth or the red and swollen nostrils flows blood or blood-stained serum containing particles of foul-smelling membrane, which excoriate the nares and lips. The air of the room is laden with a sweetish, lime-like, cadaveric fetor from the breath of the child.

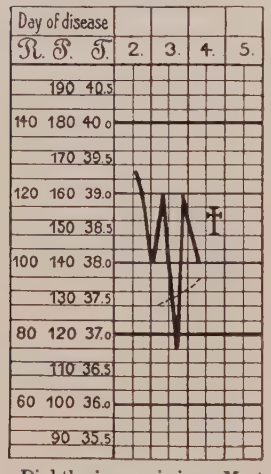
The *neck* is tremendously swollen by an enlargement of the lymph-nodes and œdema of the periglandular connective tissue, which makes the lateral contour of the neck stand out prominently.

Even at the first inspection of the *pharynx* the soft parts are found excessively swollen and the tonsils at times so greatly enlarged as to

push the elongated uvula backwards or forwards. Tonsils, uvula, pillars palate, posterior pharyngeal wall and not rarely the soft palate are covered with a slimy, grayish yellow or blackish membrane dotted with points of hæmorrhage. The swollen mucosa in its uncovered parts shows intense redness and isolated areas of bleeding. The tongue is coated heavily with a brown or blackish slimy deposit. The secretion of mucus is greatly increased. Removal of the membrane in the pharynx causes bleeding and loss of tissue; it is usually of mushy consistency and poor in fibrin, but in a few cases it is tough and gristly from a great amount of fibrin. It contains many cellular elements, diphtheria bacilli and in almost all cases streptococci, more rarely staphylococci or colon bacilli (Bernheim).

The *temperature* may remain persistently high or only slightly elevated, but as a rule it falls by the second day to or below normal. In other respects the severity of the picture remains unchanged. The patients remain apathetic and motionless and scarcely pay attention to the most urgent demands. Food and liquids are pushed aside, from dread of the pain of swallowing. Even in willing and rational children feeding is accomplished with difficulty because of the excessive swelling of the soft parts of the pharynx, and the early development of paralysis. The speech is unintelligible.

FIG. 90.



Diphtheria gravissima. Most severe form, with sudden heart failure.

The swelling in the neck is often so great that the head is held stiffly backward—Angina Ludovici. The pulse is very rapid, small and compressible.

Albumin is almost always present in the scanty urine, but the amount does not accord with the severity of the case. As a rule the albumin content is marked but only reaches or exceeds two per mille in the severest forms (Marfan).

In the majority of cases the pharynx becomes clear—with the use of antitoxin—in about eight days. Most cases show more or less deep ulcers which heal slowly with scar formation. The lymph-nodes subside and the patient enters on a long and tedious convalescence. Marked weakness, anæmia, slowing of the pulse, arrhythmia and albuminuria may persist for a long time. Postdiphtheritic paralysis occurs in almost every case.

At any time an unfavorable turn may come in the course of the disease. Anæmia advances to an intense degree, with great general weakness. The pulse becomes thready, extremely rapid and arrhythmic. The developing heart-weakness causes signs of stasis in enlargement of

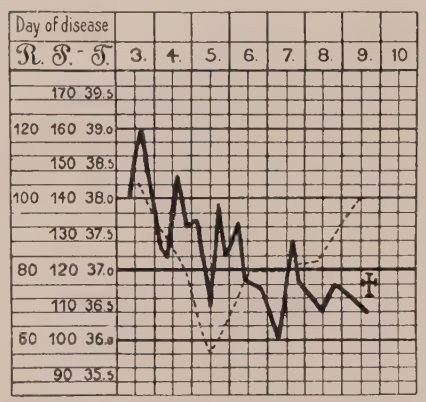
the liver and spleen, with dilatation of the right heart and at times of the left also. The apex-beat is diffuse and almost imperceptible, and the sounds are weak, especially the first which may be impure. The pulse finally can scarcely be felt. The weakness of the patient is so great that dissolution seems imminent. Towards the end of the first week or the beginning of the second, with an elevation of temperature, vomiting sets in, a certain precursor of death. The pulse falls to sixty or forty beats per minute, and the end comes about the tenth day, sometimes earlier, sometimes later, being immediately preceded by suddenly developing dyspnœa of high degree, cyanosis and an expression of great anxiety.

If the disease runs a less violent course, the cervical lymph-nodes may suppurate and the middle ear may become involved by extension of inflammation to the Eustachian tube.

The larynx and trachea are not affected in black diphtheria, as a rule, or, if so, marked stenosis rarely occurs. In such cases the mucous membrane is deeply reddened with isolated hæmorrhages and dotted with small patches of false membrane.

In some epidemics, however, a considerable exception is found to this rule, amounting to twenty per cent. of the cases of malignant diphtheria (Marfan). In these cases the local process advances in full intensity to the larynx, trachea and even the bronchi, with such rapidity that even in spite of early treatment by antitoxin and operation, the majority of cases succumb in from one to three days with obstruction and intoxication.

Fig. 91.



Malignant diphtheria. Protracted form; death from heart failure.

Not less dangerous but running a somewhat longer course is the *hæmorrhagic form* of malignant diphtheria, which is seen in about twenty per cent. (Marfan). Profuse hæmorrhages occur from the nose, mouth and pharynx which can with difficulty be controlled. There are also bleedings in the stomach, intestines and urinary tract. In the dusky skin there appear numerous spontaneous, bluish red, green or black ecchymoses, or, on very slight trauma, larger hæmorrhages. On the extensor surfaces of the knees and elbows many cases show an eruption like that of scarlet fever (Marfan). Vomiting and malodorous diarrhœa contribute to a state of great discomfort. With a profound anæmia, a progressive weakness of the heart which nothing can check, a falling temperature and a failing pulse, death occurs after a few hours or days, in coma or convulsions, or with the signs of myocarditis with or without

cardiac thrombosis. In more protracted cases pneumonia or nephritis or a general septic state may develop.

In addition to these types there may be more fulminating or more protracted forms of malignant diphtheria.

In the very rare *hypertoxic* form, as in cholera sicca, the general intoxication gains the upper hand so quickly that death occurs in twenty-four hours, before typical local changes have time to develop. The general symptoms, which appear suddenly, are heart failure, cyanosis and unconsciousness. The tonsils are seen to be moderately swollen, glistening, red and as if covered with a delicate hoar-frost (Escherich).

In the milder forms the local process is found less extensive, or only on one side, with less of a tendency to necrosis. The accompanying phenomena are correspondingly mild. Because the course is more protracted, there is time for the development of the sequels of the diphtheritic toxæmia and also for the appearance of the so-called serum disease. Secondary infections with pyogenic cocci also occur in the majority of cases; purulent inflammation of the middle ear, the glands, the joints, the bones and the serous membranes are possibilities.

The majority of these cases are saved by the timely administration of antitoxin.

2. PRIMARY NASAL DIPHTHERIA, DIPHTHERIA OF NURSLINGS AND MEMBRANOUS RHINITIS

The most frequent site for primary diphtheria, next to the pharynx, is in the nasal cavities. The fibrinous exudate may remain limited to the nose or it may spread through the posterior nares to the pharynx and mouth, or passing over the pharynx it may leap to the air-passages; in rare cases it may extend up through the lachrymal canals to the conjunctiva.

It is likely in this, as in pharyngeal diphtheria, that the lymphatic ring of the pharynx is the portal of infection for the diphtheria bacillus, and that for some special reasons not the faucial but the pharyngeal tonsil is the starting point of the process. This seems to be the case especially with nurslings in whom the acid reaction of the oral cavity acts to inhibit the growth of the diphtheria bacilli. (The fundamental cause for the extremely rare cases of pharyngeal diphtheria in the newborn may be traumatism of the oral and pharyngeal mucosa and artificial inoculation by the infected finger of the accoucheur.—Christeanu and Bruckner).

Primary nasal diphtheria begins with the *symptoms* of a marked coryza with fever, a feeling of heat and fulness in the head, and of dryness in the throat, with obstruction of the nostrils, earache and swelling of the lymph-nodes in the floor of the mouth.

The *pharynx* is dry and reddened in spots. The nasal mucosa is reddened and greatly swollen, discharging an abundant, watery, seromucus, which is sometimes bloody.

After a day or two, with an increase of fever, the *fibrinous exudate* appears, first as small, isolated, grayish spots which soon coalesce to form a thick, yellow or greenish deposit, which may become brown from extravasation of blood. The first deposits are found especially on the choanæ and the mouths of the Eustachian tubes (W. Anton). During the whole course the membrane may remain limited to the nasopharynx, but cases are seen in which the brunt of the attack is borne mainly or wholly by the anterior part of the nasal passages. In other respects the development and course are like those of secondary nasal diphtheria, with the exception that secondary complications are more frequent in this form.

Mention should be made of an appearance of *pseudo-erysipelas* as described by Monti and Escherich, starting at the anterior nares and spreading along the bridge of the nose up to the forehead.

If there is not transition to the chronic form, *recovery* occurs in eight or ten days in those cases which are not progressive or which do not develop complications. The exudate becomes limited and is separated from the basal membrane by an increased secretion of mucus which becomes admixed with the purulent discharge. According to the extent of the necrosis, recovery occurs with or without scarring.

Some *peculiarities* are seen in primary nasal diphtheria in the newborn and in infants. At the start there are only symptoms of a decided coryza: a brief elevation of temperature with a profuse, watery discharge from the nostrils; a high degree of swelling of the nasal mucosæ, making breathing difficult with a gurgling sound, while it is hard for the infant to nurse, owing to the obstructed respiration; apathy and stupor follow as a result of the lessened aeration in the lungs, with the attendant carbon dioxide poisoning. In a few days there is increased fever with rapidly developing anæmia, great prostration and speedy enlargement of the regional lymph-nodes. Nourishment is refused and a state of somnolence supervenes, interrupted by periods of excitement. The nose is completely occluded but there is a bloody, ichorous discharge. As a result of the nasal plugging, cyanosis comes on whenever the infant tries to suckle. Sometimes the membrane is visible in the nostrils. The extension of the fibrinous exudate to the pharynx or more rarely to the oral cavity may occur in two or three days with increase in the fever and in the general intoxication. Symptoms of malignant gangrenous diphtheria may arise, with death from the seventh to the ninth day, frequently in an attack of asphyxiation (Monti).

Only about forty per cent. of the cases recover. A favorable turn may come after the first or sometimes after the second elevation of

temperature, and it is accompanied by a profuse purulent discharge containing particles of membrane. It is noteworthy that the first stage may be very mild and may continue for several weeks. There is an ordinary coryza which is suspicious only through being wholly or mainly unilateral. Then with a sudden onset of severe general symptoms, that side presents the first appearance of pseudomembrane, usually on the septum.

Microscopic examination shows the same typical appearance as in pharyngeal diphtheria. In looking through many preparations only a few bacilli are found, the evidence for diphtheria being the fibrin-content with the paucity of bacteria. On the other hand, that the presence of the diphtheria bacillus is alone not sufficient to make the diagnosis of diphtheria has been shown by the researches of Trumpp, Ballin and Schaps, who found them frequently present in the nasal passages of infants who were healthy or had only simple catarrhal processes.

On the same grounds many authors hesitate to regard a peculiar kind of croupous disease of the nose, the *membranous* or *pseudomembranous rhinitis*, as a specific disease or to rank it as diphtheria. There is moderate fever, with slight redness and swelling of the nasal mucosa and a superficial fibrinous exudate. This sits lightly on the mucosa and can easily be removed, or it may fall off spontaneously, only to be followed soon by a new formation, but not causing any loss of substance or scarring. There is no tendency to involve the neighboring parts, nor are there any symptoms of general toxæmia either during or after its formation, and the only sequels are local ones (Hartmann). The only thing pointing to diphtheria is the presence—not without exception—of diphtheria bacilli.

3. PRIMARY LARYNGEAL DIPHTHERIA

It is not yet definitely proven whether there is a purely primary laryngeal diphtheria or whether in the cases in which the disease appears first in the larynx there is not an earlier specific affection in some part of the pharyngeal lymphatic ring inaccessible to inspection.

The first symptoms are those of a laryngotracheal catarrh with moderate fever. Then there develop more or less completely after a few hours, or more frequently several days and occasionally even after a week or two, the decided symptoms described on page 373. The pharynx and nose may be perfectly free or show moderate inflammatory changes, if the process is an ascending one. At the same time, however, diphtheria bacilli are found easily not only in the tracheal secretion and the particles of membrane expectorated, but also on the nasal mucosa. If the diphtheria remains limited to the larynx it runs a much more favorable and shorter course than in secondary croup.

4. CONJUNCTIVAL DIPHTHERIA

Conjunctival diphtheria is a very rare disease, usually secondary to a nasopharyngeal diphtheria advancing through the lachrymal canals. Occasionally it is primary and then it often sets up secondarily a diphtheria of the nose and throat. Impetigo, eczema and cachexia increase the predisposition to it (Marfan). According to the chief local symptoms, two main forms are recognized, the croupous and the diphtheritic. A sharp distinction is not possible, for the two forms merge into each other.

The disease always begins on the palpebral conjunctiva with redness and swelling and in both forms it may spread to the bulbar conjunctiva, and also in the severest forms to the cornea.

In *croupous conjunctivitis,* bluish or yellowish white deposits are found, sometimes thin, sometimes thick, rich in fibrin but containing few cells. When this is removed the underlying mucous membrane is seen to be red, roughened or like velvet and bleeding easily. The secretion is profuse and purulent and contains flocculi. The bulbar conjunctiva is chemotic, often covered with hæmorrhages in the form of dots or streaks, and at times it is partly covered with membrane. The cornea is clear but may rarely show a superficial clouding with a bluish film. As a rule all these appearances develop in a few days. The deposits disappear in from three to ten days, leaving a catarrhal and purulent conjunctivitis which lasts for several weeks. The cornea remains intact, hardly ever becoming permanently cloudy.

In the *diphtheritic form* the lids are very red and swollen, often with a board-like infiltration. On attempting to separate them a scanty and later profuse secretion flows out, a dirty, turbid and blood-stained serum. In the average form the grayish yellow membranes, spotted with blood or brownish discoloration, are scattered over the palpebral conjunctiva to which they are firmly attached. In the severest confluent form the conjunctiva from the edge of the lids to the palpebral folds is covered in its whole extent with a fat-like membrane, like yellowish gray rubber. Only a few of the deposits can be torn off and this causes decided bleeding with deep loss of tissue. The chemotic pale yellow bulbar cornea, at times shows diphtheritic infiltration and is raised around the cornea like a wall. The neighboring lymph-nodes are swollen and hard. There are usually more or less general constitutional symptoms with fever.

After three to five days, or in the confluent form eight days, the secretion becomes purulent, the so-called *blennorrhœiform stage.* The swelling and board-like infiltration of the lids subside and granulation tissue appears, followed by healing with scarring. The fate of the cornea depends on how soon the blennorrhœiform stage develops. If it becomes affected before this stage, it may be destroyed in twenty-four hours, either by loss of epithelium at the centre with infiltration and a step-

like loss of substances, or by a shutting off of the corneal blood supply (by pressure from the exudate) followed by a degeneration of the corneal tissue from the edge. In all the severe cases the eye is greatly injured, amounting to complete blindness in some cases as a result of scars, staphyloma or shrinking of the eyeball from a secondary suppurative iridochorioiditis.

In both of the forms general symptoms of toxæmia may supervene on the local changes. Postdiphtheritic paralyses are not rare after the diphtheritic form. In very weak children even conjunctival diphtheria alone may cause death by a general toxæmia.

5. DIPHTHERIA OF THE VULVA

In this extremely rare, usually secondary localization of diphtheria, the mons veneris, the inner folds of the groin and the labia majora are swollen and red and the regional lymph-nodes are greatly infiltrated. On the labia are seen many scattered and confluent ulcers, deep and varying in size from that of a lentil to that of a bean, covered with grayish white, firmly seated masses. Sometimes the whole vulva is covered with a single homogeneous dirty gray membrane under which deep necrosis is found. The process sometimes involves the neighboring organs.

Diphtheria of the vulva is always attended by symptoms of marked specific intoxication, and it often opens the portal for secondary infections.

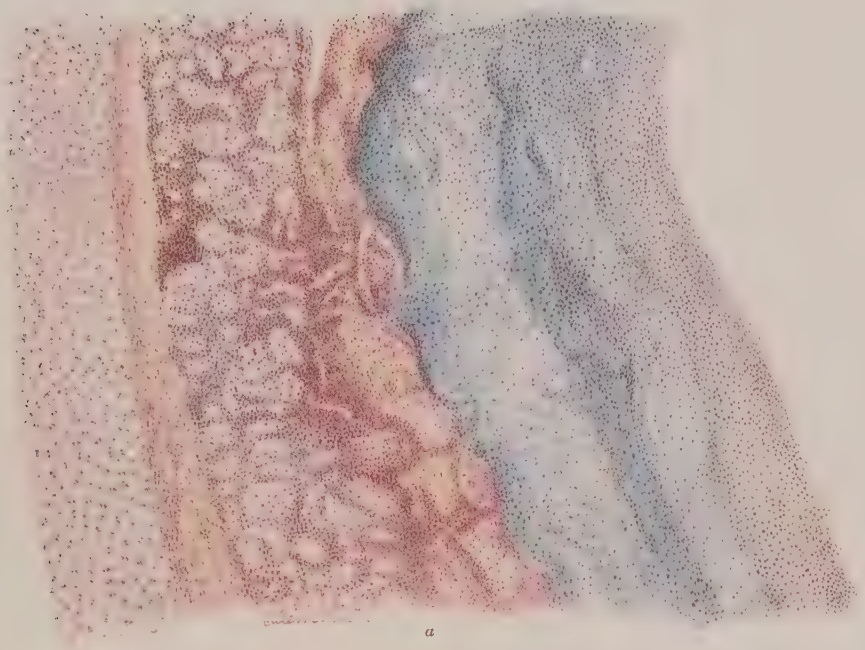
In a similar way the sexual organs in boys, with the surrounding parts may be the seat of diphtheria, but this is very rare.

6. DIPHTHERIA OF THE SKIN AND OF WOUNDS

In diphtheria of the nose, conjunctiva, or ear it sometimes happens that the irritating discharge excoriates the neighboring skin with the formation of true diphtheritic membrane. This is also found exceptionally on the sides of a tracheotomy wound. In a similar way the virus may be carried to more remote parts if, for any reason, they become denuded of their epithelium by scratches, vaccination, impetigo, eczema, erythema multiforme or other skin diseases. The affected parts of the skin show a doughy swelling and are covered usually with a thin, firmly seated membrane which may, however, change by extensive inflammation and necrosis of the skin to a thick deposit of a dirty grayish yellow or green color. From the affected parts a turbid serosanguinolent discharge issues, often of foul odor.

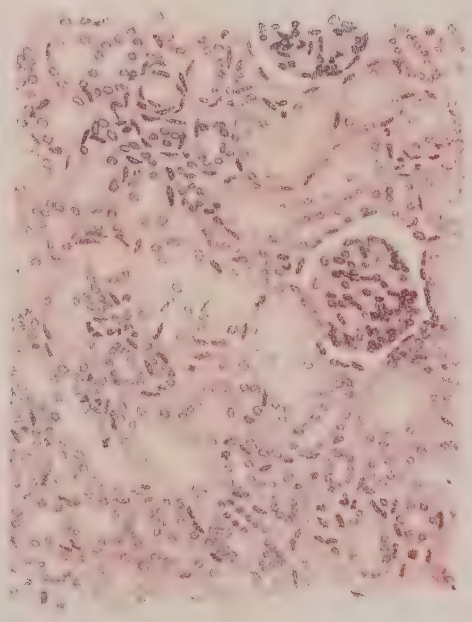
Primary cutaneous diphtheria and diphtheria of the unbroken skin are very rare. In the latter case there appear on the skin red spots, rather painful, of round or irregular outline and of varying sizes. In the centre of the spot a whitish yellow blister appears which soon becomes aggravated. Immediately after this an ulcer forms which is covered

PLATE 23.



a

b



c

a. Diphtheria of a large bronchus. The pseudomembrane lies deep in the mucous membrane tissue. The submucosa is markedly infiltrated, the mucous glands distended.

b. Interstitial myocarditis in diphtheria. The interstitial connective tissue is increased and contains fibroblasts and round cells. The œdema of the interstitial tissue and separation of muscle-fibres can be plainly seen.

c. Parenchymatous degeneration of the kidneys in diphtheria. The epithelium of the tubuli uriniferi are swollen, loosened, and fallen off. The lumen is filled with cell detritus.

with diphtheritic membrane (Seitz). In many epidemics diphtheria has been observed on the toes and fingers (Colimani, quoted by Filatow).

As bacterial toxins may be absorbed by the skin, primary cutaneous diphtheria may therefore be accompanied and followed by symptoms of toxæmia; indeed, Marfan makes the noteworthy observation that postdiphtheritic paralyses occur more frequently after the cutaneous than after other localizations of diphtheria, always appearing first in that part of the body on which the diphtheria was seated. Even with antitoxin fatal results may occur (E. Adler), being usually caused by a secondary infection with the development of sepsis.

7. DIPHTHERIA OF THE STOMACH AND INTESTINE

This is a very rare localization of diphtheria, always secondary. The œsophagus remains free but the stomach is not rarely attacked and considerable membrane is formed at the cardia, where there is a transition from the squamous epithelium of the pharynx to the cylindrical epithelium of the stomach. True diphtheria of the intestine was first observed here by Duerck.

The affection may be unnoticed during life. In other cases there is constant discomfort, pain and tenderness in the epigastrium with uncontrollable vomiting of a bloody, foul-smelling fluid, and a rapid loss of strength.

EXANTHEMS

In the course of diphtheria, but almost never before the third day of the disease, exanthems may appear, the frequency varying with the character of the epidemic.

These eruptions may be like scarlet fever, measles, rötheln or urticaria; they are transient and much like a serum-exanthem, but they are not identical with it, because they appear also in cases not treated by antitoxin. They remain a few hours, or at the most a day or two. The scarlatiniform exanthem is distinguished from true scarlet fever by the later appearance of the rash, the absence of the strawberry tongue and of the subsequent lamellar desquamation; the mottled exanthem from measles by the absence of the characteristic catarrh and of Koplik spots; the rötheln-like eruption from rötheln by the much more severe general character of the sickness.

ALBUMINURIA

Albuminuria is present on the average in about fifty per cent. of all cases of diphtheria, sometimes more frequently, sometimes less so, depending on the character of the epidemic. It is present not only in severe but also not rarely in mild cases; and it seldom appears before the third day of the disease. The amount of albumin varies greatly and

is not always dependent on the severity of the attack, and even in the same case, it may vary from day to day. In mild cases only traces are present usually; in severe cases the precipitate is abundant. An amount over two per mille is seen only in the severest diphtheria.

The amount of urine is diminished but not to the same extent as in scarlet fever. Concentration and acidity are increased while the urea output early in the attack rises greatly. Urobilinuria and indicanuria are almost constantly present (Labbé). The diazo reaction is present in the severest cases only, and these show quite regularly the features of an acute parenchymatous nephritis; great diminution of the urine, even to 200 c.c. daily, proportionately high concentration, a large albumin-content, hyalin and granular casts, epithelium, leucocytes and more rarely red blood cells.

The diphtheritic nephritis continues usually about ten or fifteen days (the albuminuria in mild cases often for only one to three days) but in protracted cases it may last until death. It is rarely accompanied by œdema and general dropsy; still more rarely by uræmia, and it almost never becomes chronic.

DIPHTHERITIC HEART FAILURE

The fatalities in diphtheria are always more or less dependent on toxic changes in the heart, some cases being pure instances of heart failure, such an event occurring either in the acute stage or in convalescence, suddenly and unexpectedly, or slowly with typical signs. The ultimate cause is still the subject of much controversy. Apparently well grounded and hard to refute is the theory of Eppinger, of a separation of the fibrils of the heart muscle from their sheath,—a myolysis from toxic œdema.

Because of the reduced strength of the heart, thrombosis and consecutive embolism may occur, immediately preceding and hastening death.

Heart failure in the acute stage is seen only in the severest form of diphtheria. It may occur without any warning or there may be premonitory symptoms of failing circulation in progressive weakness of the pulse, coldness of the extremities, cadaveric pallor with a cyanotic tint, swelling of the liver and dilatation of the heart.

Death in convalescence may likewise be sudden and unexpected or be heralded by the typical symptoms. It may occur not only after attacks of severe diphtheria apparently running a favorable course but also occasionally in relatively mild attacks. The patients may feel well and have good appetites, looking bright, improving in color and gaining strength. Then following on some slight bodily exertion, like getting out of bed, having a movement of the bowels, or eating a hearty meal, this catastrophe occurs. With great pallor and involuntary dis-

charge of stools and urine, the patients sink back quietly, but sometimes with several cries and complaints of pain referred to the abdomen (embolism of the abdominal aorta, Marfan).

In other cases, especially in older children, the heart failure occurs with prodromes of greater or less duration: the pulse becomes small, compressible, irregular, rapid, with periods of marked slowness especially shortly before death. The area of cardiac dulness is increased to the right, and at times to the left, the apex-beat is weak and the sounds are feeble, the first being impure or even rough and blowing; toward the end there is gallop-rhythm. Profound anæmia, complete anorexia and apathy deepening to somnolence set in, with unconsciousness before death. As in the acute heart failure, the end may be ushered in with restlessness and attacks of pain, and sometimes with unilateral paralyses the results of embolism (of the abdominal aorta, of the cerebral arteries, or of those of the extremities).

The period of danger may in rare cases last for a long time without these grave complications, or it may speedily subside. The improvement, however, is frequently not substantial nor lasting and the patients later succumb to an insurmountable weakness, the diphtheritic marasmus.

When the termination is recovery the albumin first disappears (Unruh), and later, the heart weakness and rapidity of the pulse. The disappearance of the albumin in such cases may then be considered a favorable sign.

DIPHTHERITIC PARALYSES

Paresis and **paralysis** occupy the first place among the nervous complications and sequels of diphtheria. They may appear early, or late in the form of the so-called postdiphtheritic paralyses. The paralysis appearing early is only localized in the pharynx, occurring in the very severe cases, from the third to the fifth day. The postdiphtheritic paralysis appears first in convalescence from one to three weeks after the disappearance of the membrane.

It is difficult to determine the *frequency* of postdiphtheritic paralysis for it is subject to great fluctuations according to the type of the epidemic. The average according to Sanné is 11 per cent., according to Cadet de Gassicourt 13 per cent., while Seitz fixes it at only 5 per cent.; if only cases that recover are considered it is probably from 20 per cent. to 23 per cent. With serum therapy, it appears to be a little less frequent; at least, when used promptly, there are fewer severe and multiple paralyses. It most frequently appears after descending diphtheria and likewise in the course of malignant diphtheria; mild cases are rarely followed by it and then only with a localization in the pharynx.

It is a flaccid, usually incomplete paralysis with partial reactions of degeneration.

There may also be other nervous disturbances, as paræsthesia, anæsthesia, rarely hyperæsthesia, neuralgias, various forms of cramps.

The affection almost always begins with a paralysis of the soft palate and pharynx, even in those cases in which the pharynx was not affected. An exception is seen sometimes, but only in malignant diphtheria. Paralysis of the eyes may follow that of the pharynx, then the lower extremities are affected followed by involvement of the upper limbs, the trunk and the neck.

The *paralyzed palate* hangs in a flaccid condition and is not moved in speaking or swallowing. As a result of the failure to close the nasopharyngeal space there are nasal voice, dysphagia with regurgitation of fluids through the nostrils, sometimes aspiration of food with attacks of coughing whenever the attempt is made to swallow. In addition, there is lessened expectoration, which adds danger to any affection of the bronchi or lungs.

The isolated palatopharyngeal paralysis subsides in ten to twenty days, occasionally earlier, or it may last a month. It may be followed in about eight days by other paralyses (in about 15 per cent. of the cases).

Strabismus comes as a result of the paralysis of the external ocular muscles, while the affection of the ciliary muscle leads to disturbances of accomodation with fatigue on reading and blurring of near objects. The pupil of the affected side reacts only to light. In rare cases the retina is involved and amblyopia occurs or even amaurosis.

Through *paresis of the legs* the gait becomes uncertain and ataxic. The weakness may be so great that walking is impossible. The patellar tendon reflexes are lessened. The arms are not often affected but in rare cases there are weakness and trembling of the hands with incapability of performing delicate movements.

In the severest cases there occurs a flaccid paralysis with diminution of electrical irritability and absence of the tendon reflexes.

It may be impossible to hold up the head because of weakness of the *muscles of the neck and back* and the patients sit in a bent-over position or are even unable to sit up. Paralysis of the facial muscles is very rare. Much danger arises if the paralysis spreads to the respiratory muscles, while involvement of the diaphragm is surely fatal. In paralysis of the larynx, which follows only after laryngeal diphtheria, aphonia and dysphagia are present with an irritating cough. Paralysis of the abductors of the vocal cords causes stenosis, paralysis of the adductors causes spontaneous extubation if intubation has been done.

Generalized paralysis almost never occurs, multiple paresis is also very rare, but their mortality mounts to 40 per cent. to 50 per cent., while the ordinary forms show 8 per cent. to 10 per cent. (Filatow).

A *fatal termination* results from paralysis of the respiratory muscles, inspiration-pneumonia, or from exhaustion in inanition. The

order of the disappearance of the paralyses, when multiple, is the same as that of their development. The convalescents frequently remain weak, anæmic and apathetic for a long time.

SECONDARY DIPHTHERIA

Some infectious diseases seem to increase the predisposition to diphtheria; either through a great weakening of the patient and a lowering of whatever immunity may be present, or by injuring the mucosa and thereby increasing the superficial predisposition. The latter is especially the case with measles and the susceptibility to diphtheria is increased so much that the secondary diphtheria always attacks those mucous membranes which bear the brunt of the *measles* attack (croup in measles with a toneless cough is always suspicious of diphtheria).

Diphtheria is apt to complicate *scarlet fever* in the second or third week, and curiously enough not in a very severe form. On the other hand the type of the disease is dangerous when scarlet fever complicates diphtheria, because the diphtheritic infection of the mucous membrane gives the streptococci always present in scarlet fever a chance to cause septicæmia.

Not less threatening is the combination of diphtheria with *whooping-cough, lobar pneumonia* or *typhoid fever* because the children are already of low vitality.

Tuberculosis seems to increase the predisposition to diphtheria.

DIAGNOSIS

In cases which set in with characteristic symptoms, especially with the decided formation of fibrinous deposits, and which show typical toxic symptoms during the acute stage or during convalescence, the diagnosis is very easy. Not rarely, however, neither local nor general symptoms are marked, and yet it is necessary in just such cases to make the diagnosis quickly because the effect of the specific treatment depends on its earliest possible use.

If the clinical features leave us in doubt, the *bacteriologic examination* will in most cases give us the desired aid. For this purpose a sterile forceps is used, preferably Löffler's (Fig. 92), to remove a piece of the friable membrane, which may then be transported in a medicine bottle partly filled with water or in a tightly closed clean envelope. The membrane is subsequently washed in sterile water to remove the outer layer of saprophytes, and then flattened out between two cover-glasses. An important characteristic of the membrane is shown by this procedure, as to whether it contains fibrin or not. If so, it does not easily spread out.

If no membrane is present, a small cotton tampon held in forceps or fastened on a stick of wood is pressed lightly against the affected part of the mucous membrane and immediately rubbed on the cover-glass

on which a drop of water has been placed. It is then dried in the air, fixed by passing through the flame three times and stained with Löffler's methylene blue. Or the cover-glass before staining may be mounted in water, not in Canada balsam, and treated with a 5 per cent. acetic acid solution in order to differentiate the Babes-Ernst granules (Cobbet).

In diphtheria much fibrin is seen, fibrillar or plate-like, as well as granular and flaky, more or less numerous cells and cell-detritus, and usually not very many bacteria; these are mainly or exclusively the diphtheria bacilli which are present in all their forms. They lie in characteristic groups of two, three or four, forming angles or parallel lines, or in large groups massed in irregular confusion within the masses of fibrin.

The same picture is seen in *mixed infections*, but with many more bacteria, often more cocci and other forms than diphtheria bacilli.

In a disintegrating diphtheritic false membrane are seen more or less structureless fibrin-masses, numerous leucocytes and swarms of staphylococci with few diphtheria bacilli.

In *nondiphtheritic deposits* there is no fibrin, or only isolated threads,

Fig. 92.

Löffler's forceps. Natural size. From Vierordt's Diagnosis.

with a great deal of cell-detritus and a great mass of the most varied forms of bacteria, covering the whole field, with perhaps a few bacilli suspiciously like the diphtheritic bacilli.

The diagnosis is certain if nests of diphtheria bacilli and fibrin are present; the presence of fibrin with a scarcity of bacteria makes it probable. If these features are absent and only a few suspicious looking bacilli are found, it is doubtful and the only procedure to clear it up is the study of a culture followed by its confirmation with animal inoculation.

By many, the microscopic examination is held in little esteem, the *culture and animal experiment* alone being considered of value. But the first method takes only a few minutes for staining, it gives certain results in many cases, and it furnishes in the number of diphtheria bacilli and their proportion to the other bacteria more valuable conclusions in mixed infections than an incompletely conducted culture method. The latter takes twelve hours and when carried out in a remote laboratory a considerably longer time; the result of animal inoculation cannot be known for three days. In addition, the results of the cultures are not always distinct. It is held by some that animal inoculation is unneces-

sary with the use of Neisser's method of double staining (one to five seconds in acetic acid-methylene blue, 2 parts, alcoholic crystal-violet solution 1 part; wash, stain for three seconds with chrysoidin solution; wash). This method, however, is equally time-consuming, for it necessitates growing the bacilli on blood serum, in an oven, for eighteen to twenty hours, and furthermore it is not absolutely trustworthy, for in the first place many true diphtheria bacilli do not show the granules, although Neisser's requirements of growth have been satisfied; and in the second place Bütschli has shown that the granules are no special peculiarity of the diphtheria bacillus.

Such being the case, *the proper method to follow is to always use the microscopic examination; if it gives doubtful results a culture may be taken, but the administration of the specific treatment should not be delayed for its verdict.*

The bacteriologic examination is to be looked on as a valuable, but with a negative result not as an exclusive, diagnostic means, and the clinical features are to be given at least equal rank with it.

DIFFERENTIAL DIAGNOSIS

1. RECOGNITION OF LOCALIZED PHARYNGEAL DIPHTHERIA FROM ACUTE NONDIPHTHERITIC AFFECTIONS

In all doubtful cases the indications of diphtheria are: (1) the contemporaneous development of a unilateral, decided coryza with a serosanguinolent discharge; (2) the contemporaneous development of laryngitis; (3) great swelling and hardness of the adjacent lymph-nodes; (4) the appearance of typical diphtheria in the family, in the neighborhood or in the school attended by the child.

Angina without Membrane.—Anginas which do not show deposits by the second day at the latest, are hardly to be suspected of being diphtheria, even if diphtheria bacilli are found on the mucous membrane. Since diphtheria bacilli are found in the throats of healthy people, a mucous membrane ought not to be considered as the seat of diphtheria if it is not altered in the typical way by the bacilli, showing epithelial necrosis and fibrinous exudate. The occasional finding of large masses of diphtheria bacilli in a starting angina makes it possible that a nonspecific secondary infection precedes the diphtheria, which will follow in a short time; or that the bacilli come from a neighboring part, inaccessible to examination (the posterior, under surface of the tonsils, the nasopharynx), but affected with the diphtheritic process.

Failure to make the diagnosis at the first examination is also rendered possible by the scanty development at the outset of the characteristic changes in the mucosa, which may be only a delicate, cloudy or frost-like deposit. Further diagnostic difficulties arise when different

parts of the same region react differently to the diphtheritic virus, the diphtheritic exudate penetrating deeply in places, but not spreading equally on the surface and so causing changes in the mucosa which are seen in other nondiphtheritic pseudomembranous affections of the pharynx.

Nondiphtheritic Pharyngeal Affections with Membrane.—These are principally anginas or stomatitis with circumscribed or diffuse catarrhal purulent or pseudomembranous deposits. In all of these a secondary infection with diphtheria bacilli is possible and must always be borne in mind.

Follicular Tonsillitis.—The swollen and suppurating follicles of the tonsils project as small yellow dots above the level of the red mucous membrane. Fever at the onset is high, with moderate swelling of the regional lymph-nodes, but there is no fetor to the breath. Usually there is no more than a family epidemic. In punctate diphtheria the islands of membrane are irregularly formed, not glistening, and the mucous membrane is frequently only a little or not at all reddened, especially in the beginning of the disease; the temperature is only moderately elevated.

Lacunar Angina.—By a deposition of catarrhal secretion in the lacunæ there appear on both inflamed tonsils small spots of unequal size, as in diphtheritic lacunar angina. The nondiphtheritic angina is recognized: (1) by the color of the deposit, pure white, glistening, changing later to a decided yellow; (2) by the limitation of the deposits to the tonsils, while in diphtheria by the second or third day the palate is attacked and through confluence the palate may be covered; (3) by the consistency of the deposit, which can easily be rubbed off and pressed out, while the fibrinous diphtheritic deposits are firmly knit and hard to detach.

Phlegmonous Tonsillitis (angina parenchymatosa). The swelling of a tonsil is associated with chills, high fever and general discomfort. On its bluish red mucosa there appears a membrane-like, oval white spot, sharply limited and made up of tenacious mucus and cast-off epithelium. Secondary œdema and excessive secretion of mucus interfere with breathing, while spasm of the masseters hinders chewing. The termination is in abscess-formation, or rarely in resolution. Transition to diphtheria is possible, but in diphtheria there is never so great a degree of inflammation limited to one tonsil, with cramp of the muscles of mastication.

Aphthous Angina.—It is very rare to see a primary localization of aphthous stomatitis on the isthmus of the fauces. The appearance is that of small, yellowish ulcers, round or oval, with slightly elevated and very red walls. If these become confluent there is a resemblance to diphtheria, but the distinction is made by the presence of the narrow

but pronounced inflammatory edge, the depression of the plaque, and the appearance of disseminated aphthæ in other parts of the mouth.

Ulcerative Tonsillitis or Vincent's Angina.—Ulcerative stomatitis varies, even when cases give the same bacteriologic results. It may give a picture so like to that of pharyngeal diphtheria that it is often called diphtheroid angina. In such a case there appears on one, usually the right, tonsil, a pseudomembrane one to two mm. thick, which may spread to the pillars and even to the soft palate, its removal causing bleeding and loss of tissue. The flow of saliva is increased and the breath has a foul odor. There is moderate swelling of the regional lymph-glands, usually of the affected side, but with no tendency to suppurate. Aside from anorexia, there is little general disturbance. The temperature may be slightly elevated, or depressed. The throat becomes clear in a few days or the necrosis may be deep enough to cause an ulcer filled with a necrotic mass; septic complications may result from this or diphtheria may develop secondarily.

The disease is distinguished from diphtheria especially by the consistency of the membrane. It is rather firm but not holding together in one piece; it consists of granular and flaky detritus and also contains remains of nuclei, fibrin-threads and numerous bacteria, especially the Bacillus fusiformis, and spirilla (Bernheim, Vincent, Dopter).

Herpetic Angina.—This is occasionally seen in children, coming on with a preliminary period of moderately high fever for one to three days, with severe headache. Then herpes form on the pharyngeal mucous membrane and break down quickly. After the vesicles have ruptured there remain yellowish depressions surrounded with an inflammatory ring, and in these a whitish deposit may occur. If these run together a similarity to diphtheria may arise. The long initial fever, *the intense headache,* the multiform appearances of the ulcers and the development of fresh crops of herpes on the mucous membrane help in differentiating the process.

The development of herpes facialis is *not* distinctive ; for it is a frequent condition, in children, well or sick, and may also be present in diphtheria.

Membrane after Tonsillotomy, Cauterization or Caustics.—A diphtheria-like membrane is seen after tonsillotomy. A mistaken diagnosis is possible only through ignorance of the history. Yet care must be exercised, for secondary infection with diphtheria is a possibility. Epithelial necrosis and subsequent ulcer-formation may follow cauterization of the mucous membrane of the mouth or throat in circumscribed spots. The history and the attendant circumstances clear up these cases.

Affections of the Pharynx in Scarlet Fever.—In this disease the picture may recall that of lacunar angina or of punctate diphtheria, or, as in diphtheria, pseudomembranes and a tendency to necrosis may

develop. In the first case, before the eruption has appeared, the onset is with vomiting (rare in diphtheria), and high fever; and the contrast of the dusky redness of the pharynx with the snow-whiteness of the tongue, and later after shedding of the coating, the characteristic strawberry appearance, all point to scarlet fever.

Diphtheroid scarlatina, which occasionally does not develop from the simple angina until the rash is fading differs from diphtheria in its limited extent—as a rule not going beyond the tonsils, and almost never attacking the larynx—in the much greater tendency to tissue-necrosis, in the very intense affection of the glands, in the absence of paralysis and in the appearance of lamellar desquamation.

Examination of the urine may furnish important aids to diagnosis. The test for the diazo reaction in diphtheria, except in the malignant forms, is negative, while in scarlet fever it is positive in 40 per cent. of the cases. Urobilinuria and indicanuria are almost constant in diphtheria and are rare in scarlet fever (Labbé).

Pseudodiphtheria.—Like ordinary aphthæ the symmetrical ulcers on the hard palate, seen in newborn and young infants, known as Bednar's aphthæ, may under some conditions resemble diphtheria very strongly. They are caused by lesions of the epithelium in suckling and swallowing or by rough cleansing. In athreptic infants these small circumscribed lesions may, by the entrance of bacteria, change to suppurating, sharply limited ulcers, which may progress in a symmetrical butterfly-fashion and cover nearly the whole of the palate. Membrane-formation may also occur in places. In the deposit are found detritus, pus cells and a great mass of the most varied forms of bacteria, especially streptococci and staphylococci. The temperature is normal or slightly elevated, and the breath has a cheesy odor.

The ulcers may be the starting-point of a septic infection; on the other hand similar necrosis of the oral and pharyngeal mucous membrane may appear in the course of an existing septicæmia (Baginsky)

While it is easy to differentiate these ulcers from diphtheria by their characteristic form and the pultaceous deposit, it is difficult to do so in the much rarer cases in which there is the fibrinous deposit on and in the mucous membrane with the formation of tough, elastic exudates, which are constantly renewed and which lead to necrosis, the process showing a tendency to spread in the same form to the mouth as well as to the respiratory and digestive tracts (pseudodiphtheritic septicæmia, Epstein). Cases running such a course, however, bear the plain evidences of septicæmia in themselves and may be recognized as such by the clinical features. The resemblance to diphtheria is even greater when coexistent congenital struma or thymus-hyperplasia causes more or less severe symptoms of stenosis (Brecelj).

Thrush.—This is a special form of stomatitis caused by the thrush-

fungus (Monilia candida). The fungus penetrates the epithelium and sets up an inflammation of the mucous membrane, showing itself in irritation, swelling and pain. The thrush colonies are round and usually granular, and if their growth is not checked, they may run together and cover the greater part of the mucous membrane with a thick, dirty-white layer. If, as is the exception, the thrush membrane is localized on the isthmus of the fauces, it may then happen through the difficulty of inspecting this part of an infant's throat that the judgment of the physician inclines to diphtheria, especially if coryza and hoarseness exist, as is frequently the case with atropic infants, with fever from some cause or other. But careful inspection of the mouth-cavity will soon show characteristic isolated thrush-colonies and, at any rate, the microscopic examination will correct the error by showing the presence of mycelium, gonidia and spores.

Syphilitic Stomatitis.—In hereditary syphilis, mucous patches may rarely occur in the mouth in the form of a whitish gray, round infiltration, sharply limited and somewhat elevated on a more or less deeply reddened base. Through considerable extension and localization on the tonsils and palate, they may resemble diphtheritic pseudomembranes, and so much the more if syphilitic coryza and laryngitis are present. And yet the patches may show plainly the presence of fissures, while all the accompaniments of diphtheria are absent, and other symptoms of lues may usually be elicited.

2. DIFFERENTIATION OF LARYNGEAL DIPHTHERIA FROM OTHER AFFECTIONS OF THE LARYNX ACCOMPANIED BY STENOSIS

The diagnosis of a laryngeal diphtheria is very easy when it occurs in the course of a pharyngeal diphtheria, but it may be very difficult if it develops after the disappearance of a mild, unobserved pharyngeal diphtheria, or if it starts primarily in the larynx, does not mount to the pharynx and if at the time of observation no loosening and expectoration of membrane have occurred. The possibility then exists of confounding the condition with a nondiphtheritic infection of the nasopharynx, larynx and trachea which may arise from some inflammatory or mechanical cause and go on to the development of dyspnœa, and even to a high degree of stenosis with attacks of asphyxia. For diphtheria, there speaks the onset with a rapidly developing catarrhal process, increase of the initial hoarseness even to complete aphonia; steadily advancing stenosis even to the maximum with attacks of asphyxia; after the attack, incomplete relief; continuation of the dyspnœa with a slight degree of increase.

In all doubtful cases, digital examination, but preferably laryngoscopic examination if possible, is to be made; sometimes the question is settled by bacteriologic examination of the pharyngeal mucus. A

negative result of this is not sufficient to exclude diphtheria; the secretion on the coughed-up or extracted tube—in case intubation has been necessary because of asphyctic attacks—is to be examined (Marfan); if no diphtheria bacilli are found in it, diphtheria may be excluded with reasonable certainty.

(*a*) *Nondiphtheritic Affections of the Nasopharynx*

Pharyngeal Angina.—Acute inflammation and swelling of the pharyngeal tonsil is of frequent occurrence in newborn and young infants. Nasal breathing is interfered with or absolutely prevented and a watery secretion flows down the posterior pharyngeal wall. In sleep it collects near the entrance to the larynx and may cause temporary obstruction to respiration. The very short duration and frequent repetitions of the attacks which do not appear when the child is awake and sitting up, as well as the usually perfectly clear voice, prevent mistaking it for diphtheria.

Retropharyngeal and Retrolaryngeal Abscesses.—Retropharyngeal abscess is seen rather frequently in infancy. It may be a suppurative lymph-node or a penetrating abscess. The primary cause in nurslings may be a lesion of the mucosa by an infected finger of the nurse. The abscess lies ordinarily at the level of the third or fourth cervical vertebræ and compresses the entrance to the larynx. There are dysphagia, regurgitation of fluids, snoring respiration and finally a high degree of dyspnœa; a swelling may also be seen externally in the corresponding region of the neck. The deep, gurgling ring to the voice (von B´kay) and digital examination separate this from laryngeal diphtheria.

Macroglossia.—Lymphangioma of the tongue, the so-called macroglossia, as seen in cretinism and myxœdema, may when inflamed cause considerable obstruction to respiration.

(*b*) *Nondiphtheritic Diseases of the Larynx*

Malformations.—The epiglottis of the newborn is normally rather deeply grooved. This peculiarity is often so strongly developed that the free edges become movable to such a degree as to narrow quite decidedly the lumen of the glottis. A congenital stridor then develops, with a gurgling sound on inspiration and difficulty on breathing amounting to attacks of stenosis when excited. The history that the symptoms have been present from birth removes all doubt about the nondiphtheritic nature of the affection, which disappears toward the end of the second year of life, with the unfolding of the epiglottis.

In very rare cases there is seen a *congenital adhesion of the anterior commissure of the vocal cords.* The glottis is therefore narrowed and so

a simple laryngitis may cause a severe stenosis. Such children have from birth a muffled, hoarse voice.

Laryngitis.—The differential diagnosis of this concerns only the first stage of laryngeal diphtheria. The main symptoms in both cases are cough and hoarseness, but their development shows characteristic differences. In laryngitis, voice and cough are loud, in diphtheria they grow steadily weaker, almost to silence. In addition, diphtheria is accompanied by increasing dyspnœa and swelling of the glands.

False Croup.—In this form of laryngitis there appear sometimes in the night, sudden and unexpected attacks of asphyxia, as a result of most acute inflammatory swelling of the subglottic region (accumulated mucus in sleep, obstructed breathing and passive congestion). The sudden onset, absence of aphonia, the relatively comfortable condition before and after the attack, all argue against its being diphtheria.

Inflammation of the Lower Vocal Cords.—This is a form of laryngitis in which a great amount of œdema may develop in the subglottic region. The onset and course strongly resemble primary laryngeal diphtheria so that the distinction is only possible by bacteriologic examination.

Œdema of the Larynx.—Injuries to the laryngeal mucous membrane by foreign bodies, burns, caustics, as well as intra- or perilaryngeal inflammatory and suppurative processes may easily cause an acute œdema leading to stenosis. The history, inspection of the mouth and pharynx and laryngoscopic examination usually render the diagnosis certain.

Thrush in the Larynx.—In very rare cases thrush may descend to the larynx and trachea, perhaps by aspiration, and the yellowish brown thrush fungi may be found in abundance (Massei, quoted by Spiegelberg). The diagnosis is made by examination of the masses removed artificially or spontaneously.

Papillomas of the larynx, the most common tumors of childhood, are congenital, or acquired as the result of laryngeal inflammation of long duration. They may, according to their position, size and number bring about a slowly increasing stenosis, or they may only occasionally close the lumen of the larynx in a valve-like fashion. In the latter instance, if a catarrhal laryngitis coexists, the condition may be mistaken for an attack of membranous croup. Of importance in the differential diagnosis is the congenital or at any rate the longstanding hoarseness.

(c) *Hyperplasia of the Thymus*

A well-developed thymus, extending deeply along the sternum, may cause great stenosis in infants, because it presses directly on the bifurcation of the trachea, where the tracheal rings are wide apart and the membranous part is extensive, so that slight pressure suffices to com-

press the trachea. Diseases causing active or passive congestion may accidentally aggravate the condition and through ignorance of the previous history diphtheria may be suspected. Examination with the Röntgen rays will establish the diagnosis.

(d) Enlargement of the Thyroid Gland

Even in the first weeks of life enlargement of the thyroid gland may act like enlargement of the thymus, if the gland is situated much deeper than usual. The stenotic râles vary in intensity according to the position of the head, that is, according as the contraction or relaxation of the sternohyoid muscles press the gland against the trachea.

(e) Tuberculosis of the Bronchial Gland

Masses of tuberculous lymph-nodes in the region of the trachea and of the bronchi may also exert pressure on the air-passages and cause stenosis. The symptoms described by Variot, Guinon and Marfan are very characteristic: dyspnœa, sucking in of the soft parts, and a loud hollow sound, especially on inspiration, which is muffled when the child is lying down. The long duration of the trouble, the weak but—so long as a recurrent nerve is not compressed—clear voice, the hoarse but not silent cough, finally the absence of false membranes, exclude diphtheria.

3. DIFFERENTIATION OF PRIMARY NASAL DIPHTHERIA FROM RHINITIS

A confounding of primary nasal diphtheria with simple rhinitis is possible only in the first stage. The presence of diphtheria bacilli and fibrinous membranes on the mucosa or in the nasal secretions, with high fever and swelling of the lymph-nodes, confirms the diagnosis and excludes simple rhinitis.

In every coryza which runs its course with high fever, prostration, swelling of the lymph-nodes and a highly excoriating, serosanguinolent or profuse purulent discharge, the bacteriologic investigation is of the highest importance.

4. DIFFERENTIATION OF CONJUNCTIVAL DIPHTHERIA FROM NONDIPHTHERITIC AFFECTIONS

Aside from conjunctival diphtheria, formation of pseudomembranes is seen in blennorrhœa, in very severe eczematous or congestive catarrh, in pemphigus, in herpes iris of the conjunctiva, and in traumatic conjunctivitis following burning, scalding and chemical irritations. The other symptoms of diphtheria and the bacilli are absent.

PROGNOSIS

The mortality of diphtheria varies greatly according to the type of the epidemic. In injected cases it is, on an average, from 12 per cent. to 16 per cent.; in uninjected cases, according to the figures of

Zucker in Styria, about 40 per cent. (in the preserum period, according to Bayeux, 55 per cent.). The number of fatalities in the separate forms of diphtheria is very varied. The figures in the Children's Clinic in Gratz (Pfaundler) in the decade from 1895–1904 gave in 1894 injected cases of localized pharyngeal diphtheria, 1.2 per cent.; for descending diphtheria (croup), 17.8 per cent.; in malignant diphtheria, 37.1 per cent. (see Fig. 81). Aside from the form of the diphtheria the termination is dependent on the age and strength of the patient, as well as the care and attention given; in brief, on the attendant circumstances. Diphtheria in nurslings is most dangerous because of the frequency of septic complications, and in children up to five years of age, because of the tendency of pharyngeal diphtheria to spread to the respiratory tract. The disease is especially threatening when it attacks radically weak and badly nourished children or those depressed by other diseases (as tuberculosis), or when it appears as a complication of measles or in the course of scarlet fever, pertussis or influenza. Everything depends on an early diagnosis and the prompt injection of the antitoxin, likewise on the strictest observance of all the rules of hygiene. It is necessary to exercise caution in giving a favorable prognosis as to the outcome, because even apparently mild cases may suddenly take a turn for the worse. Extension of the fibrinous exudate to the larynx always renders the prognosis dubious because there may be a sudden spread to the bronchial tree and death may be almost unavoidable in spite of the use of the antitoxin. The prognosis is hopeless when signs of malignant diphtheria appear: great and painful swelling of the glands with periglandular œdema, hæmorrhages into the skin and false membrane, diazo reaction in the urine, signs of heart weakness and early paralysis.

As *favorable signs* may be considered a profuse flow of saliva, a change of the pharyngeal secretion from a thick mucus to a thin fluid; also the appearance of a hyperleucocytosis three to four hours after the injection of the antitoxin. (The serum-injection is immediately followed by a hypoleucocytosis and then three or four hours later in favorable cases by a hyperleucocytosis, which is greater than that existing before the injection of antitoxin. In fatal cases the hypoleucocytosis following the injection does not yield to a hyperleucocytosis, a proof that the serum is not acting.—L. G. Simon).

PROPHYLAXIS

For efficient warfare against the plague of diphtheria there are two plans: (1) the destruction of the bacilli; (2) the closing of the avenues by which the bacilli travel.

Of the highest importance is an accurate diagnosis and a knowledge of the possibilities of infection. Very few physicians have been sufficiently schooled in bacteriologic methods or possess the necessary

apparatus for culture experiments, so in the great majority of large cities there have been established central laboratories in which examination is made of the cultures sent by physicians from cases in which diphtheria is suspected. *It is greatly to be desired that physicians should use these facilities frequently, that they should form the habit of inspecting the pharynx at every visit to a sick child. With membrane, no matter how small, and especially with unilateral, purulent, chronic rhinitis, accompanied by fever, they should study or have studied for them the exudate or discharge.* Until the report on the results of the investigation is received the physician should regard every suspicious case as true diphtheria. With such care he may be able to prevent much trouble, especially at the beginning of an epidemic. The patient and nurse should by all means be isolated. Whether the antitoxin should be given immediately depends on the special circumstances. It is better to inject unnecessarily than too late! When the diagnosis is established, all the usual precautionary measures customary in other infectious diseases are to be strenuously enforced, disinfection, forbidding visitors in the sick-room, etc., and these measures should be maintained until complete disappearance of the local symptoms, in order to avoid a spread of the infection. For the same reason, the patient, if at all feasible, should remain in one room throughout the attack.

Because contagion may have occurred before the presence of the disease is established, all children in the immediate surroundings are to receive *prophylactic injections of antitoxin.* For this a dose of 200 units is sufficient, but for children with other diseases such as measles, and for children under two years of age, it is better to inject from 600 to 1000 units.

These measures must be particularly enforced if the parents of the children come in contact in their occupations with many people, as is the case with teachers and salespeople, especially those connected with the handling of food supplies.

The physician may also be the carrier of infection. With certain precautions he may avoid receiving the infectious material, by the use of long rubber tubes on the stethoscope (with subsequent disinfection), and by standing behind the patient while inspecting the pharynx, looking down from above and thus avoiding the danger of having the patient cough in his face, and at the same time gaining a much better and deeper view of the pharynx (Fig. 93).

The immediate return of the convalescent to his family is allowed some days after the disappearance of the membrane. A separation until the bacilli have disappeared from the throat is not practically feasible, and moreover in view of their spreading to other mucous membranes where they linger much longer, it is useless. The raising of the quarantine includes a cleansing bath for the patient and disinfection of the room with formaldehyde vapor.

Not until eight days after disappearance of the membrane in uncomplicated cases is the child to be allowed to return to school. A longer exclusion from school is superfluous because the intercourse, as it ordinarily exists among school children, is not specially adapted for the transmission of the disease. Greater care is necessary with children

Fig. 93.

Inspection of the pharynx from above, standing behind the patient.

who return to such institutions as day-nurseries, because with these children "dirt-infections" are more frequent (Escherich, Feer).

The other children of the family must also be included in the exclusion from attendance at school unless they were promptly and completely isolated from the sick one, with the added protection of immunization and provided that they show no signs at all suspicious of diphtheria.

Special mention may be made of two procedures calculated to prevent the development and spread of diphtheria. Children can easily be instructed to allow inspection of the pharynx peaceably and willingly and this should be done daily in times of epidemics. They may also be taught to gargle, so as to bathe the posterior pillars and pharyngeal wall, and then in times of epidemics this may be done twice daily with a disinfecting solution, preferably with peroxide of hydrogen.

TREATMENT

(*a*) SPECIFIC TREATMENT, SERUM THERAPY

The entrance of the diphtheria toxin into the body does not have wholly harmful results, for it also stirs up a reaction by which not only the circulating toxins become destroyed, but also the organism remains immune, protected for a longer or shorter period of time against the harmful action of the specific poison.

The condition of specific immunity may be produced experimentally in animals. If a non-fatal dose of diphtheria toxin is injected into an animal, that animal, after showing symptoms of the disease, becomes immune to a much greater dose of the toxin. By means of regulated injections of steadily increasing amounts of the toxin it is possible finally to produce an immunity to any number of times the former fatal dose (active immunity).

If the serum of an animal so treated is injected into another animal, this second animal shows itself resistant to a subsequent introduction of the toxin (passive immunity); indeed, the serum from the first animal shows not only a protective action, but also a healing one, so that when injected into an animal the subject of diphtheria, it brings the disease to a standstill, modifies it and hastens recovery. For this healing action, much greater amounts of the serum are necessary than to produce the protective action, and so much the greater, the further the disease has advanced.

On this possibility of transferring the protective and healing action of the serum of an artificially immunized animal not only from animal to animal but from lower animals to man, rests von Behring's serum therapy of diphtheria.

Inasmuch as natural and artificially acquired immunity may be transferred by means of the blood and its derivatives, there must be contained in the latter specific protective substances, antibodies. Whether these exist preformed in the body or are newly developed is a mooted point. To explain the action of the antitoxin on the toxin there have been advanced three theories: a physicochemical theory (Arrhenius and Madsen), a physiological (Ehrlich), and a biological (Pauli).

Explanation of Natural and Artificially Acquired Immunity.—Accord-

ing to Ehrlich and von Behring that substance which naturally in the cells is greatly increased in amount by the action of the toxin, becomes the primary cause of healing when it is given off by the cells into the plasma of the blood.

According to Arrhenius and Madsen, the saturation of toxin and antitoxin is really a dissociation of combinations with weak affinity (Dieudonné).

According to Pauli, the toxin and antitoxin have colloidal characteristics and the very varied reactions of immunity are changes of the colloidal condition, a more or less complete neutralization of colloidal solutions (W. Pauli).

The antitoxic serum is mainly derived from horses which have been highly immunized to diphtheria. The value of the serum is found by its action toward a solution of the diphtheria toxin of known strength. That amount of serum capable of neutralizing one hundred times the fatal dose for a guinea-pig is called an antitoxin unit. If this activity is contained in one cubic centimetre of serum, that serum is called one-fold serum, but if it is contained in the hundredth part of a cubic centimetre, the serum is called 100-fold. At the present time, serum of a strength 400- and 500-fold is in the market.

In America, serums of greater concentration than those mentioned are to be found in the market. Natural serums of 700–800-fold are obtainable as are also equally strong serums which have been concentrated by chemical means. Gibson has worked out a process by which the serum globulins, with which the antitoxic principle is identified, are separated from the serum albumins and the other globulins. These antitoxic globulins are soluble in an amount of physiological salt solution from one half to one third the volume of the serum from which they are derived. In this way serums can be concentrated from two to three fold. Moreover it has been shown by Park that by the use of this concentrated and purified antitoxic globulin solution only about one half the number of cases of the "serum sickness" result and its severity is much diminished.

Without regard to the age of the patient, the *dose* should be 1000 units for localized pharyngeal diphtheria; with the appearance of toxæmia and in progressive diphtheria, 1500 units; in laryngeal stenosis and malignant diphtheria, 2000 to 3000 units. If there is no improvement after twenty-four hours, the injection should be repeated, perhaps in larger doses.

[In America physicians who have had considerable experience with diphtheria advocate the use of much larger amounts, recommending an initial dose of 4000 units for moderately severe pharyngeal or nasal diphtheria, if seen early; when laryngeal stenosis exists or if the toxæmia is decidedly evident early in the disease, at least 6000 units should be

given; if not seen before the third day 8000 or 10,000 units should be given in as concentrated a form as possible; in progressive or toxæmic cases another dose of at least 4000 units should be given in six hours and repeated at that interval subsequently until improvement is observed. Many cases apparently hopeless may thus be saved.—A. H.]

The injection may be made with any sterilized syringe holding five cubic centimetres. The most suitable sites are those parts of the skin where the connective tissue is loose, like the side of the chest or the abdominal wall. The location should be cleansed in the usual way, a fold of skin raised and the needle introduced parallel to it far enough so that the point is freely movable in the subcutaneous connective tissue. Before drawing out the needle a small piece of adhesive plaster is placed over the site of injection to prevent the escape of serum and the entrance of infection. Massage of the swelling raised by the injection is superfluous. Very often the area around the puncture is tender for twenty-four hours.

The serum hastens the melting away of the pseudomembrane and prevents a further spread of the local process. It also neutralizes more or less completely the diphtheria toxin which subsequently passes into the circulation from the affected mucous membrane. Clinically this action is noticeable in twenty to twenty-four hours. The picture resembles that of an accelerated natural recovery. The intoxication does not progress, the general well-being is improved, the fever comes down by lysis or crisis, the blood pressure rises, and the nervous symptoms disappear. Locally, the deposits are at first cleaner, glistening and then more prominent as if they were raised a little from their base, sharply demarcated and surrounded by a more or less well defined inflammatory area. On the second day they look softer and are reduced about one-half. On the third day they have wholly disappeared, or perhaps only a small particle remains. If there is a relapse and the injection is repeated, the action is similar to that in the first attack (K. Zucker).

Recovery.—An *effect* of the antitoxin is seen in all cases which live for at least twenty-four hours after the injection, and this effect is especially noticeable in the changes in the pseudomembrane. The *effect* of the serum and *recovery* are not of the same significance (Wieland), for the serum has no regenerative action on the tissue-cells attacked and destroyed by the toxin before the injection. Recovery is intimately dependent on the amount and intensity of the absorbed toxins, on the point of time at which they enter the body, and on the time of injection and the amount of the antitoxin. If a dose of antitoxin proportionate to the severity of the case is injected sufficiently early, recovery may be expected with considerable certainty under certain conditions. These are: (1) that the cases are of mild or average toxicity; in such cases the action of the toxin develops so slowly that the diagnosis and specific

therapy are not too late. In severe toxic cases, on the other hand, the toxin may be formed in such quantities and of such activity and in so short a time passing into the circulation, and the individual susceptibility may therefore be so greatly increased, that injection of the antitoxin even on the first day of the disease may not be able to prevent a fatal intoxication; (2) that the patient is not already weakened by some other disease, for in such cases it needs only a small amount of the toxin, absorbed before the injection of the antitoxin, to cause death; (3) that no septic complications are present, for the action of the *specific* remedy is only against the *specific* (diphtheria) poison, but not against other bacterial poisons, as it has not the power to combat any other kind of bacteria. In such cases therefore only partial success is to be expected, to the extent in which diphtheria toxins are taking part in the disease.

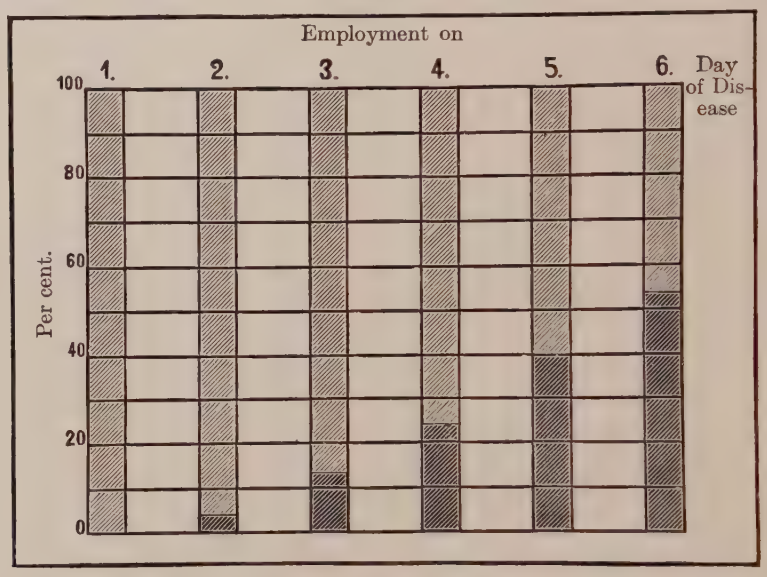
Fig. 94.

Injection of serum in the lateral chest-wall.

Because the serum exerts no regenerative nor bactericidal action, two facts stand out, which are advanced by the opponents of serum therapy as proof of its uselessness: (1) it sometimes happens that the pseudomembrane spreads for twenty-four hours after the injection, even involving intact mucous membrane. In spite of the antitoxin there may also develop albuminuria, heart-weakness and postdiphtheritic paralysis; these are symptoms which the judicious could not impute to the antitoxin, but which are to be credited to the general intoxication existing before the injection. (2) No action is observed on the diphtheria bacilli which remain much more active and virulent and are often found for months after the injection on the mucous membrane in which restitution has occurred (in one case after eighty-two days, Trumpp). It is easy to understand this, for the serum, derived by the use of the *toxin*, is able to call forth only a (transitory) artificial *toxin-immunity* and not, in the strict sense, an *infection-immunity*.

Following the conditions under which the healing action of the antitoxin is possible, an almost certain success may be expected in mildly toxic cases, the most marked success being seen in progressive diphtheria with moderate toxæmia. While it was customary in preantitoxin days to see in such cases a rapid advance of the fibrinous exudate to the bronchial tree, now the local process halts at the bifurcation of the trachea. In progressive diphtheria with great intoxication, many cases still succumb to bronchopneumonia and rapidly advancing heart failure, in spite of the antitoxin treatment. The success of the antitoxin in malignant diphtheria is much less; as in the other forms it depends on

Fig. 95.



Success of antitoxin when its use is begun on the 1st, 2nd, 3rd, 4th, 5th, and 6th day of the disease. Geh. Rat. Lingner's Monograph "Epidemics and their Prevention" ("Volkskrankheiten and ihre Bekämpfung").

the time of injection; frequently its action is only to prolong the duration of the disease.

The value of the antitoxin treatment stands out clear and sharp in *statistics*. Even if we except the fact that the mortality of diphtheria has fallen in the last decade to one-third, which may rightly be in part* attributed to a mildness in the type of the disease, there nevertheless remain the significant results of the antitoxin treatment in progressive and malignant cases. While two-thirds of the croup cases died in preantitoxin days, now two-thirds recover. Of the malignant cases formerly 80 per cent. to 90 per cent. died, now about 40 per cent. to 50 per cent. (see Fig. 80, p. 357).

*In the last decade, at least in Styria, the mortality of noninjected cases has remained near the usual, 39.5 per cent., as opposed to 12 per cent. to 13 per cent. of injected cases (Zucker).

In such a state of affairs it is the *duty* of the physician to use the antitoxin in treating diphtheria. It is furthermore his duty to give the *injection at the earliest moment*, because of the fact that recovery is so much surer the earlier the antitoxin is given (see Fig. 95); further, because of the fact that in every case of diphtheria there may suddenly occur a life-threatening extension to the respiratory tract or an equally sudden development of grave general toxæmia; finally, because of the fact that experience has shown that mixed infections are usually secondary to the diphtheria-infection.

These reasons will therefore impel the thoughtful physician not to wait in doubtful cases for the result of the bacteriologic examination, especially if the patient is very young or reduced by another disease, such as measles or tuberculosis.

In older children, with membrane of slight extent and absence of general poisoning, the injection of antitoxin may be deferred if there are other reasons for doing so, but only in such cases as may be inspected several times a day.

Much smaller doses are needed for *prophylactic injections*, because it is much easier to protect the organism against the diphtheria toxins than to combat an already-existing intoxication. 200 units are sufficient (see page 408). [In this country the average dose for prophylactic injections is at least 500 units. Doses of 1000 units are frequently used for this purpose and cases are at times reported where the disease develops in a mild form three days to two weeks after the injection of 1500 units. The U. S. Pharmacopœia gives 500 units as the average dose for prophylactic purposes.]

Because the passive immunity furnished by the injection lasts scarcely three weeks, the injection should be repeated if circumstances demand it. The value of this regulation of safety has been settled beyond peradventure by many thousands of cases.

Serum Disease.—The opponents of serum therapy assert not only that the antitoxin is useless but that it is to be blamed for the more frequent occurrence of albuminuria, paralysis and diphtheritic marasmus. This charge is just only in so far as such severe toxic cases are kept alive by the antitoxin long enough to develop the sequels of general toxæmia, while those patients would have died in the early days of the disease if the antitoxin had not been given. It cannot, however, be denied that the serum may still produce certain symptoms of disease, which cannot be ascribed to its content in antitoxin, nor to the small amount of preserving substance (0.5 per cent. phenol, chloroform, etc.) but to the horse-serum, as such. In the human system this acts like a kind of foreign substance, in a toxic way. On this account it is desirable to use a serum of the highest possible strength, in order to make the volume of the injection as small as possible. This disease is caused by

simple horse-serum as well as that containing antitoxin. Its manifestations appear after a symptomless incubation-period of from seven to fourteen days and last for a few days, if only small doses have been used, as is usual. They consist of urticaria followed by an eruption which may resemble measles, rötheln or scarlet fever, in the course of which fever develops, with swelling of the regional lymph-nodes; œdema corresponding in location to that of nephritis; at times, albuminuria; occasionally violent joint pains of brief duration with no objective symptoms in the joints; leukopenia. This disease, which has been studied by von Pirquet and Schick very carefully, depends on an individual predisposition and the volume of the serum injected. If, after an interval of from sixteen to forty-two days—or during the time when the specific products of the reaction set up by the first injection are still in the body —a second injection is given, the reaction appears immediately and is shown by an intense œdema around the site of injection, with fever and a general exanthem rarely present. If the reinjection is given after all the reactive products have been eliminated, the system then shows only a certain susceptibility to the horse-serum, the reaction is hastened, occurring after an incubation period of five to seven days (without symptoms), and is over in a few hours.

From the appearance of a specific local œdema or a typical hastened reaction, it may be confidently asserted that an injection has been given.

The differential diagnosis concerns only the exanthem. For a serum exanthem the points are: (1) the time of the eruption, seven to fourteen days after the injection; (2) first appearance of the efflorescence in the neighborhood of the site of injection; (3) enlargement of the regional lymph-nodes; (4) total absence of mucous membrane involvement.

(*b*) GENERAL TREATMENT

The general treatment consists especially of hygienic and dietetic measures. The patient of course remains in bed, warmly, but not too warmly, covered. The comfort of rest in bed is a necessity in this disease which uses up the strength so quickly. The air in the sick room is kept pure, best by removing the upper sash from a window. If the weather is so cold as to prevent this, then for one or two hours every day the window should be opened wide and the room flushed out with fresh air. If the patient is walking around at the onset of the disease, that room should be chosen which is the most spacious, brightest and sunniest, and all furnishings that would catch dust and germs are to be removed. The room is to be provided with all the furniture necessary to the care of the sick one, in order to limit the intercourse with the rest of the house as much as possible. The air of the room must be kept not only constantly fresh but moist, so as to hasten the loosening of the

pseudomembrane. Water may be vaporized in any suitable way; sometimes large sheets may be hung up and wet with a warm, weak carbolic solution. Very good service is derived from a systematic steam treatment (see treatment of laryngeal diphtheria).

The *diet* must be bland and nutritious, and because of the anorexia, as varied as possible, only small appetizing portions being placed before the patient at a time. If the pain on swallowing is great, cold food and liquids are preferable. Two or three times a day cold milk foods with not too sweet fruit juices or cold stewed fruits; between these, two or three times a day, ice-cold, diluted and acidified milk (two-thirds milk, one-third water, 15 to 20 drops of nitrohydrochloric acid) which, when anorexia is complete, may serve, alternating at short intervals with fresh fruit juice, as the sole nourishment for some time. If desire for warm food returns, in addition to milk and milk foods, cereal broths may be given, well cooked spinach, potato or carrot soup, and light farinaceous foods. If plain milk becomes distasteful, it may be mixed with malt-coffee or tea. Water may be given to drink, or toast and water with lemon juice; the addition of much sugar is not advisable. If there is fever, meat in any form, meat broths and eggs are to be excluded from the diet, but alcohol, coffee, tea, chocolate and cocoa may be allowed. Because the whole organism is depressed, digestion and assimilation are below par and care must be taken to avoid giving food too often or in too large amounts. Overloading the stomach as the appetite returns in convalescence may be dangerous.

Great care must be given to the *skin*. There should be a full bath daily, to very sick patients, in bed, while a moderately sick one may have an indifferent soap-bath of 35° C. (95° F.). A refreshing measure is sponging off with alcohol or cologne-water after the bath; or, as the child sits in the bath, after the whole body has been soaped, one part at a time may be rinsed off with cool water.

The *examination* by the physician is to be carried out with the greatest quiet, every unnecessary disturbance of the patient being avoided, especially if the heart is weak. Care must be exercised not to arouse the patient too often nor to allow him to move around too much. For eating, drinking, defecating and urinating, he should be so placed as to use as little strength as possible.

The *fever* is only to be combated when it lasts too long or is too high. The usual hydrotherapy is sufficient.

The diet may be used to overcome the ordinary constipation which arises, by giving cooked fruit freely, as well as raw, grated or pressed fruit. Enemas may be necessary.

The albuminuria as a rule demands no special treatment.

If *heart-weakness* is threatening, stimulants are to be used immediately: caffeine sodium benzoate, 0.01 to 0.1 Gm. ($\frac{1}{6}$ to 2 gr.) two or three

times a day; camphor benzoate, 0.015 to 0.05 Gm. ($\frac{1}{4}$ to 1 gr.) every hour or two; digalen three times a day, four to eight drops, finally camphor and ether injections. If necessary, oxygen inhalations must be used. Nursing and time must accomplish the rest, and the physician should see the patient two or three times a day. Later as a tonic, a cinchona preparation.

The danger of sudden heart failure, even in mild cases, lasts as long as the patients are anæmic or the pulse is arrhythmic, and rest in or on the bed should therefore be observed until these symptoms are overcome. Following malignant diphtheria, all the patients should stay in bed for two or three weeks after the pharynx has cleared. Later, they should be out a great deal in the fresh air to overcome the anæmia, which persists in a slight degree for a long time. Iron and arsenic or iron waters may be administered.

Isolated paralyses recover by themselves in a few weeks. For obstinate multiple pareses, massage, passive and active gymnastics, and faradization are to be used; the French authors (Comby) praise the favorable action of large repeated doses of antitoxin. For laryngeal paralysis strychnine is to be given by mouth 0.001 Gm. to 0.003 Gm. [$\frac{1}{60}$ to $\frac{1}{20}$ gr.] once or twice daily, or hypodermically, 0.001 Gm. two or three times a week (Henoch, Heubner). Gavage may be necessary. If paralysis of the diaphragm comes on, the phrenic nerve may be stimulated by the constant current, with the cathode between the trachea and the sternomastoid, the anode on the nape (Heubner, Escherich), with artificial respiration and inhalations of oxygen.

(*c*) LOCAL TREATMENT

Great value is to be attached to careful cleansing of the *mouth and teeth*, the latter being cleaned with a mild disinfectant three times a day after each meal, the mouth being rinsed freely. For the hourly gargling, 0.1 per cent. to 0.3 per cent. hydrogen dioxide, a weak phenol solution (one dessertspoonful of a 5 per cent. solution to a quarter-litre of water), or diluted odol (containing salol), or lemon-water. If the children are small or somnolent, the mouth should be frequently washed for them, or lemon-water given for drinking. If the children are intelligent and willing, the throats may be sprayed once or twice a day with one of these solutions. The earlier pernicious practices of swabbing, forcible detachment of the membrane and painting of the pharynx with strong disinfecting solutions are to be condemned. They are superfluous when the antitoxin is used and are dangerous in malignant cases.

A Priessnitz bandage may be applied to the neck and once or twice a day a bandage wrung out of warm oil to protect the skin.

Cleansing the nasal cavities is necessary and important in all cases of diphtheria. This may be done with the solutions already mentioned,

having them lukewarm, and pouring them in from a teaspoon or nasal douche. The head must be so held that the fluid will flow horizontally backwards and not upwards into the accessory sinuses.

Injections or irrigations with force are to be avoided, as infectious matter may be carried into the Eustachian tube.

Treatment of Nasal Diphtheria.—In nasal diphtheria irrigations are to be alternated with insufflations of menthol, 0.5 Gm. (8 gr.), sodium sozoiodate 1.0 to 2.0 Gm. (15–30 gr.), powdered sugar 20.0 Gm. (5 dr.). The eroded areas on the nose and upper lip are to be protected with an ointment. If the obstruction of the nostrils is so great

Fig. 96.

Steam-room. In the adjacent room there is a copper boiler, heated by gas and discharging steam through a copper pipe in the wall into the steam-room; an automatic regulator keeps the water at a constant level. Maximum capacity, six children. Children's Clinic, Gratz, Prof. Pfaundler.

that drinking is impossible one or two drops of a 1 per cent. cocaine solution may be instilled into the nostrils. For subsequent use a weaker solution is to be recommended,—cocaine hydrochlorate, 0.5 Gm. (8 gr.), boric acid 4.0 Gm. (1 dr.), water 200.0 c.c. (4 oz., 2 dr.) in order to reduce the swelling of the mucous membrane quickly.

Treatment of Diphtheritic Otitis.—On account of the constant danger of the spread of a nasopharyngeal diphtheria to the tube and middle ear, the ears must be examined daily and if redness of the drum-membrane is found, a warm solution of thymol, 0.1: 50.0, or phenol-glycerin, 1: 10, should be dropped in the canal. The latter acts more

surely but renders difficult the judgment on the inflammation because a little clouding occurs. Paracentesis has the usual indications. If there follows a purulent discharge, a 1 per cent. to 2 per cent. solution of hydrogen dioxide should be dropped in hourly.

Fig. 97.

Improvised steam-room.

Treatment of Conjunctival Diphtheria.—In the stage of board-like infiltration there should be copious irrigation with normal salt-solution or boric acid solution, with ointment to the lids, and lukewarm compresses (no ice). In the blennorrhœic stage, the treatment is the same as for any other purulent conjunctivitis; if the cornea is not affected,

nitrate of silver may be used sparingly, in a 1 per cent. to 2 per cent. solution, or protargol, 5 per cent. to 10 per cent.

Treatment of Cutaneous and Vulvar Diphtheria.—Sublimate compresses are to be applied until the membrane has disappeared, then borated iodoform powder.

Treatment of Laryngeal Diphtheria.—As soon as signs of laryngeal involvement appear, steam-inhalations must be begun at once. With them, about 40 per cent. of antitoxin cases may avoid operation. In many children's hospitals there is a special steam-room. Fig. 95 shows such a one in Pfaundler's Clinic.

Sometimes the children are given the inhalations only periodically, for an hour at a time. In private practice, Richaud's plan may be used of hanging wet clothes in the room, or submerging glowing irons or hot bricks in pans of water, or in dwellings of the poor pouring water on the hearth-plate. The best plan is to use a steam apparatus as recommended by Escherich, F. Müller, Trumpp, which projects the steam against the patient's face. To increase its effect sheets may be hung over the bed, improvising a steam-room (see Fig. 97).

To favor the elimination by the skin, hot, moist compresses may be placed around the neck, or mustard poultices. If stenosis sets in, a hot bath followed by a sweat-pack is to be recommended. During the pack a mixture of lime-blossom and elder tea may be drunk.

If, in spite of this and the antitoxin treatment, no improvement is evident, but the stenosis increases and the children become exhausted, operation is necessary to furnish free access of air to the lungs. The bloodless procedure of O'Dwyer's endolaryngeal intubation may be chosen, or the cutting operation of tracheotomy.

Intubation has so many advantages over tracheotomy that it must be considered first. One of the main advantages is that it is bloodless and permission to perform it is always obtained, while tracheotomy is often forbidden by parents who dread the knife. In addition, intubation consumes no more seconds of time than tracheotomy does minutes. It can be done without assistance and without good illumination, two things necessary for the proper performance of tracheotomy. There is no danger from bleeding or from wound-infection. The duration of treatment is considerably shorter because there is no wound to heal after removal of the tube. Its results in hospitals are equally as good, about 65 per cent. recoveries (Siegert); while in private practice they are better than tracheotomy (Trumpp). Accidents during the operation (shock, heart failure, pushing down of the membrane) are rare and only to be feared with clumsy, prolonged attempts. On the other hand, disturbances of swallowing, coughing up of the tube or plugging, and furthermore, the development of pressure-ulcers with their sequels furnish more or less severe difficulties. Disturbances of speech such as chronic

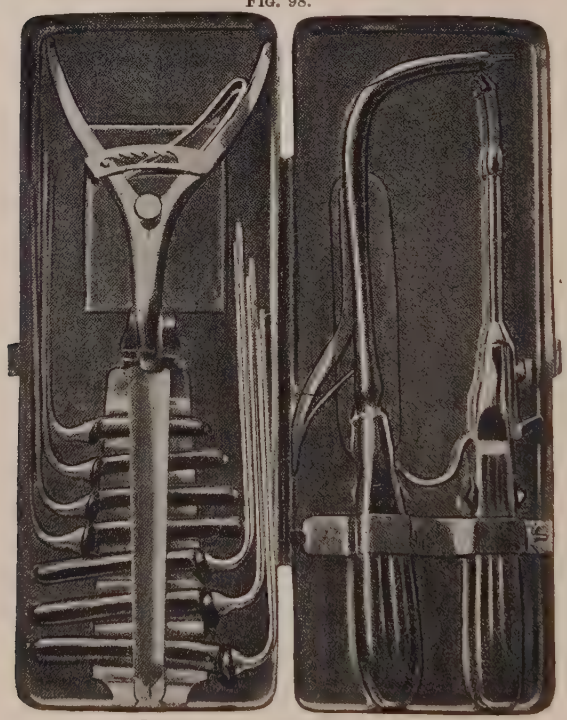
hoarseness, shortness of breath, etc., are on the other hand more frequent after tracheotomy than after intubation (Pfaundler, Trumpp).

Intubation is contraindicated if the conditions present are such that free passage of air through the tube cannot be expected or if a favorable introduction of the tube is for any reason impossible. In such cases tracheotomy must be resorted to instead, and the trachea must be opened above or below the isthmus of the thyroid. If at all possible, tracheotomy is to be done with a tube already in the trachea, as it is much easier to find the trachea then than when it is empty. Dangers during the operation are emphysema, asphyxia and bleeding; subsequently the same complications may arise as in intubation, increased by the possibility of infection of the wound and secondary hæmorrhage, but dysphagia, coughing up and obstruction of the cannula are far rarer.

TECHNIC OF INTUBATION

An intubation outfit comprises six or seven tubes of varying length made of metal, hard rubber or elastic material; an instrument for inserting the tube, one for extracting it and a mouth-gag. Fig. 98 shows an ebonite set. The tubes are introduced through the mouth into the larynx and left there until the diphtheritic inflammation has receded, usually about three days. The patient should be wrapped from the neck to the feet in a blanket, and he may be intubated while lying in bed or held on the lap of an assistant, who holds the child's legs firmly between the knees, with one hand steadying the mouth-gag and with the other holding the head firmly in moderate extension (see Fig. 99). The tube is introduced along the left index finger as a guide, which reaches deep in the pharynx and opens the entrance of the larynx by holding the epiglottis up against the root of the tongue, so that this is pushed up and forward. Points to be observed

Fig. 98.



Intubation set with ebonite tubes.

in the operation are: (1) *The instrument must be introduced exactly in the middle line* in order that it may not catch in any of the different lateral folds of the pharyngeal mucous membrane. (2) *As the epiglottis is passed, the handle of the introductor must be raised* in order that the tube does not glide into the œsophagus over the root of the tongue which half overhangs the entrance to the larynx. (3) *The handle is again to be lowered*

Fig. 99.

Manner of holding the child during intubation.

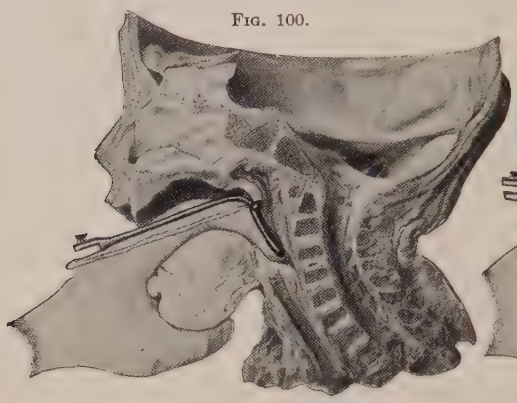
after the entrance of the tube into the larynx in order to prevent traumatism of the anterior wall of the larynx by the end of the tube (see Figs. 100, 101, 102).

Extubation is accomplished by means of a thread tied to the head of the tube and carried over to one side of the mouth, or if this is bitten through, the tube may be drawn out by the extubator, a special instrument for the purpose.

TECHNIC OF TRACHEOTOMY

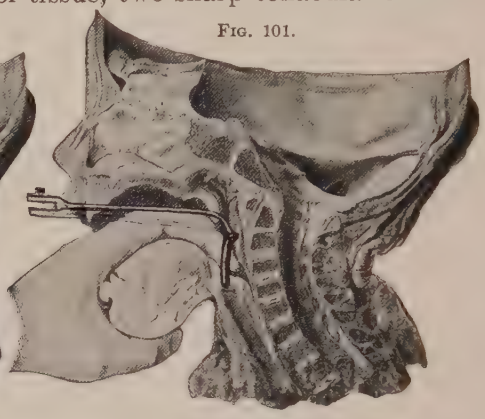
A tracheotomy set contains: one scalpel for the skin-incision, one surgical and one anatomical forceps for separating the connective tissue, one grooved director for raising the fascia, two blunt hooks with several teeth for holding apart the layers of tissue, two sharp tenacula for hold-

Fig. 100.



Intubation. Step I.—The index finger of the left hand holds up the epiglottis and serves as a guide for the tube; the right hand is lowered.

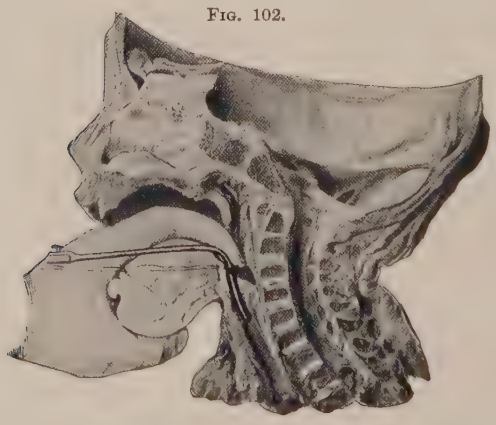
Fig. 101.



Intubation. Step II.—The tube enters the upper part of the larynx; the right hand is raised.

ing up the trachea, one sharp-pointed knife for opening the trachea, one blunt-pointed knife for enlarging the tracheal opening, two or three cannulas with movable shields, as suggested by Luer or Hagedorn, or two plain cannulas, as suggested by Bruns, artery forceps, scissors.

Fig. 102.



Intubation. Step III.—The tube passes the glottis, the right hand again being lowered.

The patient should be wrapped in a blanket (as for intubation) and then laid on a table with the neck put gently on the stretch, which may be conveniently accomplished by wrapping a bottle or other article in a towel and placing it under the nape of the neck. An assistant should have charge of the anæsthetization—which is superfluous with a high degree of carbon dioxide poisoning—and he should also watch carefully to prevent any lateral displacement of the neck. The preliminary steps of cleansing are the same as for every cutting operation. The incision, as with all subsequent separation of tissues, should be in the median line; extending for at least five centimetres, in superior tracheotomy to the thyroid isthmus, in inferior tracheotomy to the sternum. The subcutaneous connective

tissue is to be torn apart with blunt instruments, such as closed hæmostatic forceps, the next step being, with the help of a grooved director, to divide the superficial cervical fascia and the linea alba of the sternohyoid muscles, visible through it. The next steps depend on whether the tracheotomy is high or low. In *high tracheotomy*, the deep cervical fascia lying directly under the muscles must be separated by a transverse incision from the lower edge of a tracheal cartilage and then bluntly dissected from the trachea and drawn downwards with the thyroid gland enclosed in it, thus laying bare the trachea.

If the *low tracheotomy* is being done, the separate layers of the cervical fascia are to be divided longitudinally on a grooved director until the thyroid gland is exposed. After division of the lowest layer, the partly exposed trachea is to be drawn up by two tenacula and freed from any remaining areolar tissue. A pointed scalpel is now introduced into the trachea until a whistling sound tells that the lumen is opened, when the incision is to be enlarged sufficiently (1 to 1.5 cm.) to admit the cannula. (In a low tracheotomy the opening is to be placed as high as possible.) As soon as respiration is easy, the cannula is to be introduced and held in place by tapes around the neck. The wound should be carefully dusted with iodoform and protected by lint or rubber protective from the tracheal mucus.

Difficulties may arise during the operation from a large or adherent thyroid gland, a large thymus, numerous distended veins and rarely also from arterial anomalies.

After forty-eight hours the *cannula should be changed* for a clean one. To prevent collapse of the soft parts they should be held up with tenacula, and an elastic catheter (with lateral holes) should be introduced through the cannula into the trachea, to serve as a guide for the removal of the old and the introduction of a fresh one. After a day or two a speaking cannula may be introduced and by closing the external aperture a test may be made of the degree of patulousness of the larynx. When the child has slept quietly at night with a closed speaking cannula, then it may be entirely dispensed with and the wound allowed to heal under an occlusive dressing.

Following a secondary tracheotomy after a long intubation, it is wise to hasten removal of the cannula as much as possible, in order that the breathing in the natural way with the air-pressure which this exerts in the larynx may hinder the formation of a stricture (v. Ranke).

When extreme peril exists, Fischl's instantaneous method may be followed by which after the deep cervical fascia is reached, the trachea is drawn forward by two tenacula, and opened by one cut passing through all the soft parts including the isthmus of the thyroid. The cannula, held ready, is immediately thrust into the gaping opening, only the cannula ending in a closed point being suitable. Pressure controls the

bleeding which starts as respiration is established. Even quicker is the procedure of L. G. Simon and Schinzinger which consists of fixing the trachea against the vertebral column and opening it with one single incision through skin and soft parts. The index finger of the left hand is immediately pressed into the wound to check the bleeding while the cannula is guided along the nail as the finger is withdrawn.

Less dangerous than this mode of tracheotomy is *cricotomy*, which, however, has the disadvantage that it always causes speech-defect, an interference with the formation of the voice.

MUMPS—EPIDEMIC PAROTITIS

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THIS epidemic inflammation of the parotid gland is, as the name indicates, of a contagious nature. For the most part it attacks completely healthy individuals. Thus we have to deal with a primary, idiopathic parotitis, as distinguished from those inflammatory processes of the gland which occur in the course, and as a result of, other diseases of an infectious character, and which may be grouped as secondary or metastatic parotitis.

Epidemic parotitis manifests itself in so striking a manner that neither the early period of its first accurate description (Hippocrates) nor the numerous appellations given to it by the laity need excite any surprise (Mumps, Ziegenpeter, Tölpel). These popular designations owe their origin to the peculiar appearance of the patient caused by the swelling of the face. The humerous concepts of these names indicates also that the laity has long recognized the benign nature of the disease.

Pathogenesis, Anatomy.—The infection of the parotid most likely starts from the mucous membrane of the mouth, the microorganisms invading the gland through Steno's duct, and exciting an inflammation.

According to a limited number of anatomical observations, the inflammation is confined to the interacinous tissue while the epithelium of the glandular canals remains normal. The periglandular and interacinous cellular tissue appears to be infiltrated by a serous or serofibrinous exudation. If a mixed infection with pyogenic bacteria from the mouth does not complicate the specific process, suppuration of the gland does not occur. However, when there is extreme swelling, a pressure necrosis may occur, here and there sharply demarcated from the other tissue. But in most cases the process is entirely free from local complications and when the exudation is absorbed, complete restitution takes place.

Local Symptoms.—The most striking symptom is the swelling in the region of the parotid gland, which enables the physician to make a diagnosis even at some distance from the patient. The location of the

swelling at times causes a striking displacement of the lobe of the ear upwardly and laterally, a position which, to a certain extent, is pathognomonic of parotid swelling. This horizontal displacement of the lobe of the ear, however, may be frequently wanting, so that we should not attach to it too much importance. The dimensions of the swelling are subject to great fluctuations. While at times the swelling in the fossa situated between the ramus of the lower jaw and the mastoid process is confined to the region of the parotid, at other times the swelling may exceed these boundaries and spread either upwards or downwards.

Fig. 103.

Mumps (left side) in an eight-year-old boy.

Thus it may happen that the swelling may spread upward even to the orbit and laterally, in a diffuse manner, over the whole cheek down to the submaxillary region. In such a case the entire half of the face appears swollen, the fissure of the eyelid narrowed, and the conjunctiva inflamed. In some cases the swelling may extend to the neck and even down to the clavicle. In bilateral parotitis, the swelling of the neck may join the median line and merge, the neck assuming the shape of a sausage-like tumor. If the face is involved to a slight degree, the neck appears much broader than the face.

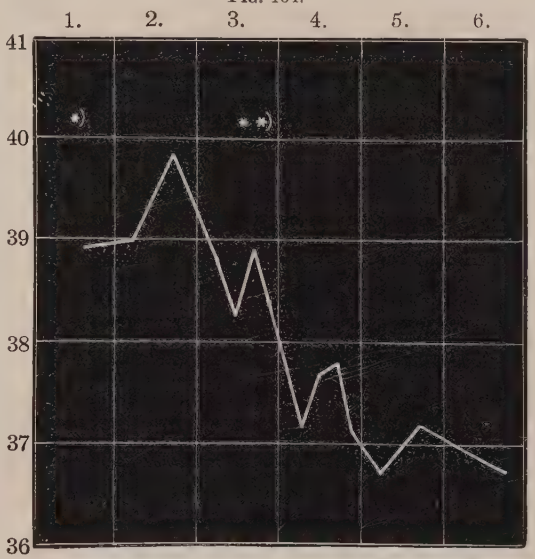
The skin over the tumefaction is tense and shiny; its color is only in rare cases slightly reddened. The tumor itself feels doughy or tensely elastic.

These swellings disfigure more or less the faces of children; and it is evident that the higher degrees of the swelling cause various inconveniences. In mild cases there is frequently no sensitiveness to pressure in the parotid. In more marked swellings there is localized pain, especially when the children open their mouths to permit an inspection of the throat, to take food or to chew a hard morsel. Thus in many cases children experience difficulty in eating.

An inspection of the mouth and throat in most cases reveals normal conditions. At times there is a simple stomatitis and pharyngitis, whose occurrence is favored by the lack of attention to the mouth, which is neglected on account of the pain felt in opening the jaws. In extreme cases the swelling spreads deeply downwards, overcoming the natural resistance of the deep-seated cervical fascia and we observe that the pharyngeal entrance is very much narrowed by the protrusion of the lateral pharyngeal walls and the tonsils.

The diffuse extension of the swelling to the neck produces moreover a certain stiffness in the posture of the head. The pressure upon the adjacent ear, especially the cartilaginous meatus and the Eustachian tube, diminishes the delicacy of hearing and causes a pricking sensation in the ear, a symptom met with quite frequently at the very beginning of parotitis. If the tumor continues to press for a long time upon the facial nerve, a transitory facial paresis may occur (Falkenheim). The effects of local pressure, in severe cases, may extend even to the larynx and trachea, the disturbed circulation of the blood causing a local œdema and so leading indirectly to a pronounced laryngeal stenosis.

Fig. 104.



Temperature chart of a moderately severe case of mumps.

As a rule, the salivary secretion, which, in a definite affection of the parotid would receive a good deal of attention, remains normal. Only rarely do disturbances in the way of increased or diminished flow of saliva manifest themselves. Nor does the saliva, chemically, show any qualitative or quantitative alteration. The diastatic ferment and the amount of potassium sulphocyanide correspond to normal.

General Symptoms.—The local symptoms, which are of an exclusively mechanical nature, are accompanied by a series of general phenomena of which fever is the most prominent. In contrast with other infectious diseases of childhood, this fever exhibits a wholly irregular course, so that contagious parotitis has no typical temperature curve. Thus in some cases, fever may be absent; in others an elevation of temperature occurs before a swelling of the parotid is seen, but in most cases an elevation of temperature coincides with the beginning of the swelling of

the gland, dropping at times to normal after a few days, like a crisis, even before the recession of the local symptoms. Sometimes fever accompanies the disease and slowly diminishes with the subsidence of the parotid swelling. Just as irregular as its course is the height of the fever. More frequent than a high elevation of temperature up to 40°–41° C. (104°–106° F.), which naturally may be accompanied by apathy, somnolence, and delirium, are the low temperatures 38°–39° C. (101°–103° F.). If after a few days the inflammation attacks the opposite parotid, the temperature generally again rises. If, during the convalescent stage another increase of temperature occurs, complications may be suspected unless it indicates a relapse, which, however, is very rare.

At the height of the affection, in severe cases, there is a swelling of the spleen and of the regional lymph-nodes.

Prodromes.—A few days before the appearance of the parotid tumor the children become cross and contrary; they lose their desire for play, their appetites decrease and at times they complain of headache. Very frequently these general symptoms are accompanied by gastric disturbances. Nausea and vomiting ensue, and diarrhœa may occur at the very beginning of the disease and may continue during its whole course; in fact cases in which diarrhœa attains a considerable degree of intensity are not rare. The intensity fluctuates according to the prevailing character of the epidemic.

Course.—The symptoms usually preceding the parotid swelling, are grouped as the prodromata of mumps. They are not at all characteristic and apart from certain local pain there is manifest a feeling of tension in the typical location. The prodromata hardly ever last longer than one to three days, and may be wanting entirely.

It is only with the occurrence of the parotid swelling that the disease proper begins. The duration varies, depending essentially upon the intensity of the swelling. Thus in light cases the disease lasts two to three days; in cases of moderate severity five to eight days. But it may at times continue longer, so that the process in severe cases, especially when the second parotid is involved, may not cease until weeks have elapsed. If no complications ensue, the process runs along smoothly as a rule, leaving behind no functional disturbances.

The disease proper is preceded by an incubation stage, lasting eighteen to twenty-two days. The very length of this incubation period is to a certain extent typical, so that families with many children sometimes do not get rid of the mumps for half a year.

Contagiousness and Disposition.—Parotitis is a peculiarly epidemic affection, as shown by its spread in families, educational institutions, schools, in towns, cities, and provinces. Almost without exception the infection takes place directly, from child to child, but cases have been reported in which a direct transmission could be positively

excluded and an indirect infection through third persons or objects (even letters) must be assumed. Such cases would indicate that the exciting agent of parotitis has a greater resisting power than the contagion of the acute exanthemata. Statistics show that the disease appears more frequently during the cold than during the warm season. There exist no relations to other infectious diseases in the sense of an increase or decrease of predisposition to parotitis during the course of or after convalescence from other infectious diseases.

With the recovery from parotitis the body almost always acquires a specific immunity against this disease which, as a rule, continues through life, but some cases of genuine relapses have been observed and reported (Gerhardt, Hochsinger, Schilling, Nirmier, etc.).

Children between the ages of four to fifteen years have the greatest disposition to infection, whereas those under two years are rarely affected. Primary parotitis in infancy is exceedingly rare. Falkenheim reports such a case in an infant seven months old, and White one in a newborn child. We may, accordingly, assume that the infant possesses against parotitis a peculiar natural congenital immunity as he does against other infection; or accept Soltmann's explanation that the incomplete development of the parotid and the narrowness of its duct offer unfavorable conditions for the infection.

The character of the epidemic is of especial interest. It has already been stated that in certain epidemics, gastro-intestinal phenomena are conspicuous. But its contagiousness too, is dominated by the "genius epidemicus," parotitis in many epidemics being marked by an uncanny infectiousness, whereas in others the affection appears in only isolated cases; so that the brothers and sisters of an infected child are spared. In many epidemics, regularly only one gland is involved, whereas in others there is a bilateral parotitis. As in other infectious diseases, the character of the epidemic varies, especially with regard to complications.

Complications.—The complications and sequelæ of parotitis are as rare as they are diverse. The best known, because most peculiar, complication is that described by Hippocrates, a unilateral orchitis (orchitis parotidea). This complication is observed beyond the age of puberty more often than in childhood. Henoch never saw a single case. However such well authenticated cases have been reported that there can be no doubt concerning the close relations of the two organs in parotitis. In the course of certain epidemics orchitis appears much more frequently than in others. At times, strange to say, the testicle alone is specifically affected, while the parotid remains free. In quite an analogous manner, although still more rarely, the genital tract of girls is involved in the parotitis process. Included in these rarities are unilateral swelling of the mamma, of the labia majora, and of the ovaries. Perhaps we would discover these benign complications more frequently if we

paid particular attention to them. There have been reported a few cases of simultaneous swelling of the thyroid, thymus, and lachrymal glands.

Very frequently the submaxillary gland is involved along with the parotid, swelling so much that it may be felt as a hard tumor at the angle of the lower jaw. Sometimes the submaxillary gland is specifically affected and the parotid is spared (so-called submaxillary mumps).

Beyond the involvement of glands, complications on the part of other organs especially during childhood are interesting and noteworthy. Foremost among these is nephritis (Henoch, Mettenheimer, etc.). The period of its appearance varies. Most commonly it sets in during the stage of convalescence, concomitant parotitis and nephritis being very rare. The nephritis has almost always a hæmorrhagic character and must be distinguished from those symptoms of renal irritation which, under the aspect of a febrile albuminuria, not infrequently manifest themselves in the course of parotitis. Its course is as a rule benign.

Other complications to be noted are disturbances of the central nervous system, such as convulsions, delirium, and severe psychoses, attended sometimes by transitory dementia and loss of memory (Heubner).

In other cases, somatic disturbances of the nervous system, such as rigidity of the pupils, paralysis of the ocular muscles, monoplegia, and sensory disturbances have been observed after parotitis. All these phenomena point to the existence of cerebral focal lesions, the severest form of which, under the picture of a post-parotitic meningo-encephalitis, may result in death (Maximovitch and Gallavardin).

More frequent are complications of the auditory organ. Otitis media may be understood from the nature of the parotitis itself and from the proximity of the infection (Steno's duct and the Eustachian tube). But even without preceding inflammation of the middle ear parotitis may be attended with severe labyrinthine affections, associated with deafness, vertigo, and intense headache, and as experience teaches, yield a very unfavorable prognosis.

Grancher and Longuet were the first to report cases of endopericarditis after mumps, and subsequently many cases were reported. Finally may be mentioned the rare complications on the part of the joints. These behave much like gonorrhœal and scarlatinous articular affections, but as a rule have a milder course (Lannois and Lemoine).

Etiology.—The etiology of parotitis is as yet by no means sufficiently explained. True, the character of the disease presupposes the existence of a specific pathogenic factor, but the bacteriological findings at hand are few, deficient and unsatisfactory. Deserving of great appreciation are the investigations of Bein and Michaelis (1897), according to which, in mumps, motile diplostreptococci were demonstrated in the buccal secretion, in pus, and once in the blood; and F. Pick (1902) in cultivating micro-organisms from the fluid obtained by puncture of

the inflamed parotid, which he identified as the organisms of Bein and Michaelis. On the other hand, Schottmüller, after puncture of the gland under the most careful precautions, found the secretion to be perfectly sterile. The demonstration of transmission failed in every case.

Diagnosis.—The diagnosis is made from the local symptoms. In the differential diagnosis there need be considered only such other glandular swellings in the region of the ear and under the angle of the jaw as appear either spontaneously or associated with inflammatory processes in the buccal cavity (for instance, Pfeiffer's glandular fever). But if we take into consideration the typical seat of the parotid tumor, which corresponds exactly to the topographical situation of the gland, and if even with intense swelling a redness of the skin is wanting, we may, even before the suppuration of other lymphatic tumors, safely avoid confounding them with mumps and vice versa. Secondary and metastatic parotitis are considered elsewhere. Great diagnostic difficulty is encountered only in those cases in which the submaxillary gland alone is specifically affected, the diagnosis here must be based only and exclusively on the course of the disease and on data in the history.

Prognosis.—In spite of the number and severity of complicating contingencies the prognosis is nevertheless favorable. But for an adequate estimation of the prognosis we must contrast the greatly preponderating number of cases running their course without leaving any trace with the rare occurrence of more serious complications, which nowadays are of considerable casuistic interest.

Prophylaxis.—The prophylaxis is confined to the isolation of the sound children from those already affected. However, in view of the benign character of the affection and in view of the fact that parotitis in childhood is more easily endured than in advanced age, such precautionary measures are for the most part unheeded. I believe that it is contrary to the general welfare to permit the further spreading of the affection by the non-observance of these simple rules, apart from the fact that with increasing age the disposition to infection decreases considerably. Isolation therefore, as far as practicable, should be recommended. The duration of the contagiousness is six weeks.

Treatment.—The treatment is local and symptomatic. In order to relieve the tension of the skin, warm oils or emollient salves may be applied on a cotton dressing loosely over the swollen parts. In obstinate cases, in order to facilitate absorption within the inflamed gland, the affected portion should be anointed with iodide of potash ointment or iodovasogen, once or twice a day. The mouth should be carefully cleansed, in order to prevent stomatitis. Moreover, rest in bed must be ordered as long as there is fever; confinement to the room until there is no inflammatory glandular swelling, and, in order to regulate the digestion and to avoid local pains, a liquid diet.

TYPHOID FEVER—ABDOMINAL TYPHUS

BY
PROFESSOR R. FISCHL, OF PRAGUE

TRANSLATED BY
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BY this name we designate an acute specific infectious disease primarily localized in the bowel, whence the causative bacilli enter the lymphatics and the blood. (It is now believed that the localization in the bowel does not take place until after the invasion of the blood circulation.) It is met with in childhood about as frequently as at other periods of life.

With regard to the *mode of transmission*, it was formerly thought to be really contagious, but this of such slight degree that nobody cared particularly to isolate the patients. Certain observations, however, communicated especially by Dr. Robert Koch from his careful study of an epidemic, warn us to have more regard for the contagious factor—not only to disinfect, and remove dejecta, urine and sputa, which for some time have been considered as the most important sources of the disease, but also to isolate the patient. Even the early investigators warned against infection through the water used for drinking, culinary purposes, or bathing (a sad example of which Prague has for years been furnishing), yet as Koch points out, this is to be less regarded than those mild cases which clinically are hardly noticed; healthy individuals whose evacuations contain typhoid bacilli, and must be appreciated as disseminators of the disease. We should not however follow him in this curt disregard for hitherto prevailing views, although we may infer from his observations and from his protective measures thus successfully established that besides the hitherto combated sources of infection there are others that should be considered.

Where typhoid fever is endemic we observe often enough that infants, even those that are nourished exclusively on their mothers' or nurses' breasts, become affected and infect their nurse. In such cases the infection must have taken place through other than the usual channels, and the water used for bathing has been suspected. Cow's milk too, may be instrumental in spreading the disease, infected by water used for the purpose of diluting the milk, or by flies carrying the bacilli, etc. Cases of intra-uterine infection, generally resulting in death and

expulsion of the fœtus, have rather a casuistic interest. Transmission through suction is asserted by some, denied by others, and as a rule is difficult to prove, in that an affected nurse can infect the baby in many ways. On the other hand, there are cases in which nurses suffering from typhoid fever of moderate severity have taken certain precautions and have attended the infants during the whole course of the fever without infecting them,—an experiment too daring to be imitated.

The *cause of the disease* is the typhoid bacillus, described by Eberth and first cultivated by Gaffky,—a cylindrical bacillus with rounded ends, and provided with a chaplet of cilia, presents lively transverse and longitudinal movements. It easily takes the aniline dyes and rapidly gives them up again, grows on the usual culture media, is facultative anaërobic, and ceases to grow at a temperature above 46° C. (115°F.). The appearance of the cultures is not very characteristic, that on potatoes being the most striking one, a moist, lustrous, mucous coating, looking like parchment. A knowledge of the appearance of bouillon cultures is important, since these show a diffuse turbidity within 12 to 24 hours, but, with transmitted light, exhibit darker stripes, resembling the vein-like markings on marble. In appropriate culture media the typhoid bacillus does not produce gas nor ferment sugar, nor cause indol formation, nor does it coagulate milk.

The great powers of resistance and endurance of the bacilli assumed on the strength of experiments made by Janowski and others, by virtue of which they are able to live in the water and in the ground for a long period and even resist freezing, are controverted by Koch on the strength of his own investigation. He admits, however, that they will withstand desiccation, which does not hurt their vitality. A consideration of the clinical features of the disease and the post-mortem appearances points to the production of a soluble poison by the bacilli, but the production of such a poison has as yet been impossible.

Immunization experiments and serotherapeutic trials will be discussed in the chapter on treatment.

It is important to differentiate the typhoid bacillus from the bacterium coli, which, morphologically, culturally, and, as recent investigations made by G. Sallus show, genetically, is closely related to the bacillus typhosus. The bacterium coli, according to the same investigator, is said to form the same aggresin (in the sense of Bail) as the typhoid bacillus. If so, the identity of the two species, as already assumed by many, becomes very probable. Likewise, reports from various sources, made during the last few years concerning paratyphoid bacilli, show that in this group of schizomycetes there exist many similarities and affinities, and that the cultural differences are for the most part insufficient for a separation of the species.

The cultivation of the bacillus may be made from the living or the

dead subject. The demonstration during life has a great prophylactic value, and we may justly hail it as an essential advance that, by the method elaborated by Drigalski and Conradi, we are able to cultivate the typhoid bacillus from the dejections during the very first days of the disease and to separate them from other bacteria. The former methods, such as those of Elsner, Piorkowski, and others, were inadequate. By this means it was possible for Koch to recognize early and isolate the cases during the epidemic at Gelsenkirchen. Other places where the organisms may be found in the living are the spleen (from which the germs are obtained by puncture, a procedure that cannot be recommended) and in a very high percentage of cases the rose spots where they may be sought for without danger to the patient.

In the cadaver, the surest places to find the bacillus are the spleen, the mesenteric lymph-nodes and the gall bladder, where, according to the observations made at the Prague Pathological Institute and confirmed elsewhere, bacilli may be almost always demonstrated.

Besides the culture methods which enable us to differentiate the typhoid bacilli from morphologically similar organisms, and which are based essentially on the absence of gas formation, of indol production, and of coagulation of milk, we possess quite a reliable method of recognition in agglutination which will be discussed later.

Pathological Findings.—While the post-mortem findings in an adult are quite characteristic, those in children, especially in the first years of life, are much less typical; ulceration for the most part is wanting and the changes are confined to a slight infiltration of the agminated and later of the solitary follicles, such as occurs in severe enteritis. Moreover, we find in the earlier stages catarrhal swelling and hyperæmia of the mucosa in the lower part of the ileum and in the region of the ileocecal valve, at times extending also to other portions of the small intestine, and considerable infiltration of the mesenteric glands corresponding to the altered portions of the bowel. It is, however, the soft and enlarged spleen that particularly indicates typhoid fever. Other alterations that may be mentioned are a parenchymatous degeneration of the liver and kidneys, muscular degeneration of the heart, œdema and hyperæmia of the meninges and cerebral substance, lobular and lobar pneumonia are almost constantly present, hyperæmia of the bronchial mucous membrane, and such secondary infectious processes as suppuration of the middle ear, gangrene of the cheeks, suppuration of the parotid, purulent joint affections, etc.

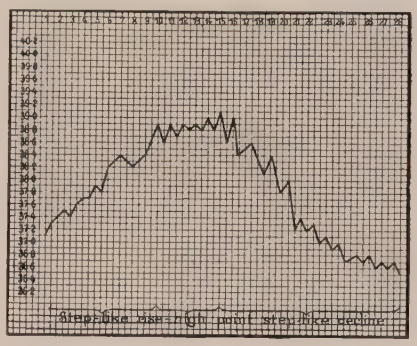
We see from the above that the typical necroses, ulcers, and cicatrices are missing, and, as Marfan forcibly remarks, we frequently have presented, especially in infants, a pathologico-anatomic picture more indicative of a septicæmia and a complete explanation only follows a bacteriologic examination.

Course of the Disease.—In childhood the course of abdominal typhoid is relatively mild, and the mortality correspondingly small. During the time I have been preparing this article and in spite of the great prevalence of typhoid in our city, I have been unable to obtain any material from post-mortem examinations of children to have pictures made.

Filatow states that the mortality of children varies between 3 and 10 per cent. against 17 to 25 per cent. in adults, yet severe epidemics occur, for instance one reported by Guinon in Paris with a mortality of 17.5 per cent.

Moreover, the course of the disease is shorter in children, the duration of the several stages being less and symptoms which later are highly dangerous, as intestinal hæmorrhages and perforation, are exceedingly rare, there being no ulceration, or only rarely and this only in older children. The onset as a rule is unnoticed, showing itself in different ways, disposition to sleep at an unusual hour, restlessness at night, loss of appetite, mild disturbances of digestion such as eructations, moderate vomiting, and constipation; thus inconspicuously, the disease is slowly ushered in until the fever with its somewhat characteristic steps is present. The latter may be divided properly into three stages—a period of gradual ascent of temperature (called stadium incrementi by Filatow), continuous fever, and defervescence. The first period exhibits an evening exacerbation of temperature each morning higher than the preceeding morning and then a steady rise of fever. In the second stages the difference between morning and evening temperature is only slight, .5 to 1.5° C. (1° to 4° F.), and in the third stage the temperature descends to the normal in the morning while in the evening there is a slight increase, and this gradually diminishes. The aggregate duration of the fever in light and medium cases is 2½ to 3 weeks, of which 3 to 5 days may be allotted to the first stage and as many days to the third stage, while the period of continuous fever lasts 10 to 14 days.

FIG. 105.



Normal temperature curve in typhoid fever.

As a matter of course, there are numerous deviations from the type just described. There may be a longer duration of the fever (up to 40 days and more), the so-called "formes prolongées" of Cadet de Gassicourt, as well as a shorter or abortive course; sudden onset with sharply rising temperature, observed especially in quite young children; a critical fall of the fever; the so-called inverted type, in which the morning tem-

perature is higher than the evening. For the most part the fever remains at a mean height in the first years of life not exceeding 39° to 39.5° C. (102°–103° F.), but occasionally there are considerable elevations of temperature up to 41°–42° C. (106°–107.6° F.), which are usually well borne by the youthful patients as is fever generally. A sudden drop of the temperature, with simultaneous bad appearance of the patient, whose face becomes pale and pointed, is as a rule indicative of intestinal hæmorrhage or perforation and is, therefore, a sign of bad omen.

The *frequency of the pulse* increases slowly and not excessively, so that the rate closely corresponds to the fever or is even slower. Only in case of the occurrence of some dangerous complications, in cardiac weakness and in the death agony does the pulse become thready and hardly perceptible. Dicrotism is frequently present, but on account of the smallness of the arterial tube it cannot be easily detected by the palpating finger. During the period of convalescence, the pulse frequently becomes slower and at times irregular.

Concerning the *blood pressure* we have investigations made by Carrière and Doncourt, from which we learn that at the beginning of the affection the arterial tension drops from 13 or 14 to 8 or 7, but during the second phase slowly rises from 9 to 28. During the period of defervescence and convalescence, comes a second decrease of pressure, followed slowly by a return to normal conditions. Increase of blood pressure may occasion intestinal hæmorrhages, pulmonary congestion, delirium, etc. Myocarditis is not always accompanied by a decrease of the blood pressure.

The younger the child, the less the accompanying *nervous symptoms*, which for the most part are confined to apathy and restlessness at night. The typhoid state which is so characteristic in the adult with highly flushed or pale cheeks, injected conjunctivæ, dull expression, etc., is rare. At most a hyper-excitability prevails, such as tossing about in bed, tremor of the hands, hyperæmia of the face, uncanny lustre of the eyes or finally even convulsions. A furibund delirium, alternating with deep stupor, points to a cerebral disturbance especially when rigidity of the neck and back muscles, picking of the bed clothes, deep sighing, grinding of the teeth, and other symptoms characteristic of meningitis set in. During convalescence aphasia may occur as I have seen in a case observed jointly by Escherich and me, which presented also symptoms of idiocy. Similar cases have been reported. In another case under my observation after defervescence, there occurred an eclamptic attack lasting a day and a half with resulting imbecility. Delirium from inanition, melancholic depression, transitory paralysis of various muscles, etc., are by no means rare sequelæ of grave typhoid and all of these point to a severe intoxication.

The *loss of appetite* (though usually not absolute), the *high fever*, the *diarrhœa*, and the insufficient night's rest lead in children to great emaciation, which at times becomes extreme, but during convalescence conditions quickly improve. Often the *hair* falls out and is replaced by a thin, lustreless aftergrowth; but, in contrast to the adult, rarely is any permanent harm done. The *finger nails* exhibit transverse furrows and flutings; often the nails drop off, and new ones grow in, but not, as Feer believes, such as are characteristic of scarlet fever. Under the trophic disturbances we note desquamation of the skin such as described by Hamernik, in the form of branlike or large scaly exfoliations of the trunk and of the extremities, while the face, hands, and feet remain unaffected. Rachmaninow observed this desquamation in one-third of all the cases of typhoid fever in children that came under his notice. It appeared either during the stadium decrementi or not until after the temperature reached normal and continued from 8 to 14 days. The severity of the disease had no influence on its occurrence.

Patients frequently have a peculiar craving for certain undigestible foods, obstinately rejecting what liquid food is offered them, and their aversion lasts as long as the fever. Frequently as early as the period of deferescence, and regularly during convalescence, ravenous hunger is present which demands firmness on the part of the physician and his assistants, since the foods which are permitted do not satisfy the appetite and more food must be refused.

In the typhoid of childhood, the *tongue* often presents a characteristic appearance. It seems to be narrowed, covered at first with a gray transparent coating and later with a thick white deposit, sharply contrasting with the dark red border and the clean moist tip. There are, however, as I have seen repeatedly, cases in which during the whole course of the disease the tongue showed no coating or at most only a slight, breath-like turbidity. The clearing of the tongue begins at the tip, which gives rise to the so-called "typhoid triangle" with its apex towards the root of the tongue. A dry tongue, looking as if it had been smoked, or covered with a thick black coating, is met with only in severe cases in which also the lips are dry and fissured, presenting bleeding rhagades encrusted with a dark brown deposit. A foul odor issues from the mouth; the bases of the teeth are covered with a slimy yellowish brown mass; and the nostrils, which the patients are constantly picking as they are their lips, appear ulcerated and incrusted. On the other hand, mycoses, which in the severe typhoid of adults are a frequent and prognostically bad symptom, are rarely met with in children.

Swelling of the parotid, according to Biedert, is always indicative of a severe mouth infection and a malignant course; it usually occurs towards the end of the second week, and undergoes suppuration, provided the patient lives long enough.

Pseudomembranous anginas occur in severe typhoid fever developing during the course of the disease and rarely constituting the first symptoms, though I have observed this in three cases and it has been described by others. Of different significance is a pharyngeal affection described by E. L. Wagner as "angina typhosa," with the development of flat ulcerations on the palatal arches and likely to be regarded as a primary affection. In children this angina is met with relatively seldom, but instead of it we frequently notice a circumscribed injection affecting the palatal arches and the epiglottis, with some œdema of the mucous membrane. Mya, who studied more closely the nature of angina mycosa, was able to cultivate typhoid bacilli from the ulcerations in the pharynx, which were not present in mere catarrhal forms.

Vomiting is more frequent than in adults, often inaugurating the disease or accompanying it. If associated with constipation,—an occurrence by no means rare in the typhoid fever of children,—it suggests meningitis. *Abdominal pains* are usually wanting or if present, not violent, which is in correspondence with the absence of intestinal ulceration. Gurgling in the ileocecal region is usually wanting, whereas it may be found in a large number of divers non-typhoidal intestinal affections, so that no diagnostic value can be attached to it. *Meteorism* is never very considerable, sometimes it is absent, and at times there may be retraction of the abdomen. *Diarrhœa*, as a rule, sets in rather late. In rare cases, some of which I have observed, the disease begins with the symptoms of a violent colitis, attended with tenesmus and bloody-mucous stools. But, as already stated, in most cases the thin, fluid evacuations in moderate number (3 to 5 in 24 hours) and following a constipation, do not appear until the second week. *Constipation*, however, may continue throughout the course of the disease, as I have seen repeatedly.

The *diarrhœal discharges* have the characteristic, pea-soup appearance, and if left standing in a glass vessel present a lower stratum consisting of bright yellow and whitish flakes. From these, bacilli may be cultivated in doubtful cases according to the method of Drigalski and Conradi. An exceptionally profuse diarrhœa may cause the children to become very much emaciated, and it may continue at most 12 to 14 days, though the usual thin typhoid stools are replaced much sooner by solid evacuations or it may be that constipation occurs during convalescence. Involuntary evacuations are always an unfavorable symptom indicating an unusually severe course of the disease, especially when succeeded by deep stupor and paralysis of the sphincter so that the intestinal contents steadily ooze from the gaping anal orifice.

Intestinal hæmorrhages and *perforations*, with their sequelæ, are met with almost exclusively in older children as in the young there is little anatomical alteration, necrosis and ulcerations being absent; but when these complications occur they have the same dangerous signifi-

cance as in adult life. The symptoms of intestinal hæmorrhage are sudden collapse, with rapid depression of bodily temperature, cold sweat, pallor of face, cold nose and extremities, smallness of the pulse, followed in a few hours or by the next day by the passage of black or bright red masses per anum. Perforation takes place only in the later stages of the disease (third to fifth week); it begins with violent vomiting and singultus, to be soon followed by collapse and a rapidly developing, painful peritonitis. But peritonitis may ensue without intestinal perforation as a result of an extension of the process, by contiguity, to the serosa, and the prognosis in such cases is less unfavorable.

One of the most important symptoms and, in doubtful cases after the second year, of decisive aid in the diagnosis of typhoid fever, is *swelling of the spleen*, the frequency of which is about the same as in adults. The spleen enlarges at an early period and grows steadily with the development of the fever, becoming three or four times its original size, particularly in its long axis. However, meteorism or overlying by bowel may prevent its recognition by percussion, while the more reliable palpation with the hand and fingers flatly placed on the abdomen and pressing gently under the costal arch, may be valueless either on account of the softness of the spleen or the tension of the abdominal muscles. Certainly we must never content ourselves with a single examination for the determination of an enlarged spleen is of such decisive diagnostic moment. During the period of declining fever, the spleen becomes rapidly smaller, usually attaining its normal dimensions at the beginning of convalescence.

On the part of the respiratory organs we notice *epistaxis* relatively seldom and only in the early stages of the process; except, however, in those severe cases in which it is a phenomenon of the hæmorrhagic diathesis. *Bronchial catarrh* is a usual accompaniment of typhoid in children, and is localized mostly in the larger and middle branches of the bronchi. Where expectoration is scant and cardiac action slight, a hypostasis may result in the lower portions of the lung and, as a result of this, the percussion sound becomes duller and there are moist râles with soft bronchial breathing (so-called sub-bronchial respiration). At the same time there occurs a slight cyanosis with increased frequency of pulse and respiration, dilatation of the alæ nasi and a call upon the auxiliary respiratory muscles, symptoms all suggestive of an encroachment on the respiratory area. A rise of fever would occasion the suspicion of the development of genuine bronchopneumonic foci. Such an occurrence is a serious complication, at least protracting the disease, and often causing a fatal termination from asphyxia, pulmonary œdema or paralysis of the heart muscle. The development of a *croupous pneumonia* may likewise become a serious complication usually occurring at the height of the fever or at the beginning of its decline. In the latter

case the temperature will again shoot upwards, and the pneumonia may become localized in different portions of the lungs, especially in the upper lobes and cause a loud bronchial breathing, typical crepitant râles, severe dyspnœa, and intense general phenomena, or may as a migratory pneumonia successively affect adjoining portions of the lung. *Pneumonia* is a serious complication of typhoid. The form of typhoid fever described by Gerhardt in adults as "pneumotyphus," setting in under the aspect of a pneumonia, followed by typhoid symptoms, is very rare in children. It is only a few weeks ago that I had the opportunity to observe a case of this kind for the first time. The patient was a child twenty-one months old taken ill suddenly with rapidly ascending temperature, and a small pneumonic focus developed in the left upper lobe, which some days later resolved without a fall in the temperature; rather the fever continuing with enlarged spleen, diarrhœa, roseola, in short with all the symptoms of a rather severe typhoid fever that terminated favorably.

Gangrene of the lungs is a complication that rarely occurs and only in intensely severe cases. More frequently we meet with *pleuritis*, with either serous or purulent exudation, caused either by the typhoid bacilli or, more frequently, by a mixed infection. A *latent tuberculosis*, localized in the peribronchial lymph-nodes may be aroused by the fever and especially by the concomitant bronchial catarrh, and may manifest itself by a continuance of fever, which usually presents irregular fluctuations at times of a hectic character, as well as by increasing cough, dyspnœa, and evidence of foci of infiltration in the lungs.

Laryngeal complications, which in adults, especially in the course of certain epidemics, are frequent and always serious occurrences, are rarely observed in the typhoid fever of children. They may appear as *laryngitis*, corresponding anatomically to an infiltration of the mucous membrane; or as ulcerations analogous to those described as occurring in the pharynx; or even as a *laryngeal perichondritis*, with cartilaginous necrosis and abscess formation. Clinically this complication is manifest by aphonia, rasping croup-like cough, dyspnœa, fits of suffocation, and, if it begins in the third or fourth week, by an increase of fever. A form of typhoid, beginning with laryngeal symptoms and occurring in children, has been described by Schuster as "laryngotyphus," the laryngeal symptoms continuing during the whole course of the disease. Fibrinous inflammation of the larynx and paralysis of the laryngeal muscles have been reported.

With respect to *cardiac complications* endocarditis and pericarditis may occur, but they are more rarely encountered in typhoid fever than in the course of other infectious diseases.

Of the symptoms on the part of the skin, the *rose spots* are the most conspicuous, equaling the enlarged spleen in diagnostic value. They

appear five to ten days after the beginning of the fever, usually confined to the abdomen and back, less often except during infancy they are diffused over the entire body. The exanthem consists of pale-red slightly elevated papules of the size of a pinhead which disappear on pressure with the finger. The eruption comes out in several series and vanishes after a short time. The fact that the eruption cannot always be easily demonstrated is distinctly indicative of typhoid fever, the often scanty efflorescences must be carefully looked for or they may be overlooked. In a case under my observation the eruption was confined to a small group of lichen-like nodules in the right loin. From flea bites, which they resemble very much, these efflorescences are distinguished by the absence of a central point corresponding to the bite. Their number is no criterion of the course of typhoid fever; but a bluish color, instead of the customary rose, points to a serious infection. There are, however, cases in which the rose spots are wanting during the entire course of the disease.

While during the first days of the disease the skin appears very dry, it is possible that later, especially at the initial remission of the fever, a profuse perspiration with miliaria may occur; this is devoid of any diagnostic or prognostic significance. Recently Auché and Letrelle have described cases of disseminated cutaneous gangrene which occasions bluish red plaques with ecchymotic centres or abscesses of the skin. The same author and others have also observed pustules and numerous cutaneous and subcutaneous abscesses. I have witnessed similar cases, the severest of which was that of the son of one of my colleagues, whose whole body was covered with numerous walnut-sized pus foci. It is evident that such complications aggravate and protract the disease. There occur also polymorphous erythemata, predominantly localized around the joints, and caused by a micrococcus closely related to the diplococcus hæmorrhagicus (Leroux and Lorrain).

Decubitus, quite frequent and justly feared in adults, is rare in children, and is met with only in the severe and neglected cases. The decubitus is usually over the sacral bone, and never spreads extensively or deeply. Complications with *erysipelas* is an exceptional occurrence though it was observed by Escherich and myself, in a case where it started from the scrotum: this child also presented evidences of idiocy and aphasia. On the other hand, *herpes labialis*, which formerly was regarded as negative of typhoid fever, but indicative of pneumonia, is not at all rare in children.

Paresis of the lower extremities is sometimes observed. It retards convalescence, but as a rule, it disappears without leaving any permanent traces. I have already mentioned a case of eclampsia with subsequent idiocy. In such a complication we have evidently to deal with a localization of the process in the meninges or in the cerebral cortex.

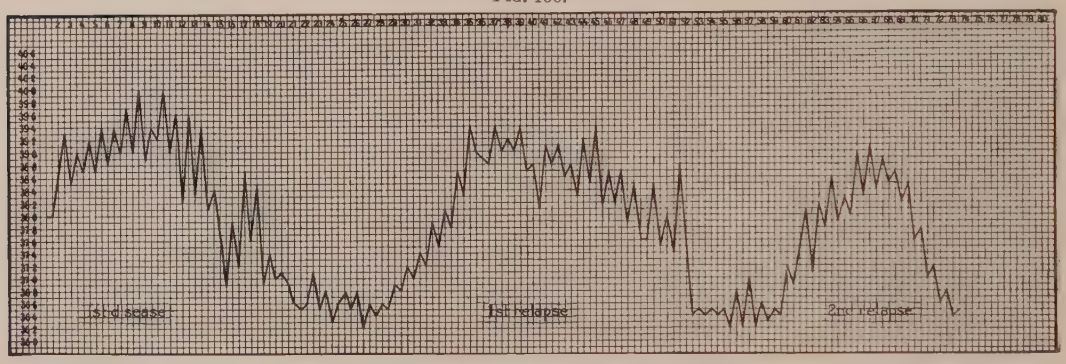
Several authors have spoken of the demonstration in cases of meningitis of bacilli in the cerebrospinal fluid obtained by lumbar puncture.

Among the involvements of the *organs of sense,* apoplexy of the retina described by Bouchut may be mentioned, likewise otitis media, whose causation is evidently connected with the mouth infections which accompany typhoid and are rather frequent. During the period of convalescence deafness exists frequently, but is only transitory.

The *blood* exhibits hypoleucocytosis, reduction of the amount of hæmoglobin and of the number of eosinophilous elements. These findings may at times be utilized for purposes of differential diagnosis in initial pneumonia. I cannot substantiate the fibrin reaction as stated by Rosenthal that no fibrin network forms in the fresh preparation of typhoid blood, whereas in pneumonia, meningitis, and other affections with accompanying leucocytosis, a fibrin web may develop in the course of half an hour.

The *urine* usually is scant, often contains albumin, less frequently

Fig. 106.



Relapses in typhoid fever.

casts and renal epithelia. Sometimes it exhibits the character of nephritic urine, and there is a form of the affection designated as renal-typhoid in which these symptoms manifest themselves at the very beginning and dominate the disease. As already stated, typhoid bacilli frequently occur in the urine. Ehrlich's diazo reaction usually proves positive at the height of the process. From the time of its appearance, its intensity, and duration we may, with certain precaution, draw prognostic conclusions. On the part of the *sexual organs* we observe rarely in girls a pseudomembranous inflammation of the vagina and gangrene (noma) of the labia.

Having described the course of light, medium and malignant cases of typhoid fever in childhood with their complications and sequelæ, there remains to give a short survey of some particular and peculiar features of the disease. Foremost among these are the abortive cases, distinguished from ordinary typhoid by their short duration, and accom-

panied either by light or severe symptoms. Next come protracted cases in which without complications or sequelæ, the fever may persist for five weeks and longer. Finally we have feverless or afebrile cases, by all means the rarest anomaly of the morbid process. These forms, frequently overlooked or falsely interpreted, play a rôle in spreading the infection that must not be underestimated. Their recognition has been materially facilitated by the modern methods of cultivating the bacteria from the dejections and by Widal's agglutination reaction.

Relapses in children are scarcely rarer than in adults. They may occur during the period of defervescence, forcing the temperature again upwards; or set in after a brief afebrile interval. The relapse may equal in intensity and duration the first onset or exceed it, or be less, or repeat itself many times (see temperature curve in Fig. 106) thus protracting the duration of the disease considerably. In a case reported by Comby, the fever relapsed six times and lasted fully four months.

Typhoid fever in infancy occupies, in a certain sense, a separate position. On the strength of my own experience I can not confirm the assertion made on various sides that the affection is exceedingly rare during the first half of life. True, the symptoms are of a rather vague nature; yet the course of the temperature curve, which in point of constancy and regularity, is not encountered in other febrile intestinal affections of this age, will lead to the right scent, and the usually profuse eruption of roseola should remove any doubt. Marfan, Gerhardt, and recently Forget, consider the prognosis of the affection at this age as especially bad, its mortality, according to the last-mentioned author, being 50 per cent. The latter claim, however, is contrary to my observation, for in a dozen cases of typhoid fever in infants there was only one with fatal termination. True, these infants were all breast-fed, which may have a certain influence on the prognosis. Likewise, the extensive intestinal alterations advanced by various writers, which may lead to perforation, I have never been able to observe in the necroscopic material at the Prague Pathological Institute.

The **course** and **termination** generally speaking is likely to be shorter and more favorable than in adults, but they exhibit great variation. The height of the fever indicates the gravity of the case to a lesser extent than the tempestuous beginning of the phenomena with sharp ascent of the temperature, rapidly developing disturbance of the sensorium, pallor of the face, dryness and fuliginous coating of the tongue and teeth, fissured lips, intense prostration, feeble and frequent pulse, etc. But even in such cases the conditions are not quite so unfavorable as in later life the two most dangerous contingencies, intestinal hæmorrhage and perforation, being of rare occurrence. Ambulatory typhoid in children, especially from the lower strata of society, is by no means rare, yet I have had repeatedly patients from the better classes brought

to my office who had been feverish for some time and in whom I was able to determine the fully developed disease. Many cases of this kind may suddenly terminate unfavorably, as Biedert and others have observed.

The **diagnosis,** on account of its mild course and the vague symptoms during the first week, is usually quite difficult and may be established only by exclusion. The course of the temperature, which should be taken every three or four hours, the steadily increasing size of the spleen, and the eruption of roseola, both of which symptoms are scarcely observable before the end of the first week of fever, finally clear up the diagnosis. However, very frequently—and any practitioner of average experience will agree with me—a differential diagnosis from other febrile conditions of childhood may be exceedingly difficult. Foremost among these I mention miliary tuberculosis, which may equally stealthily set in, at first presenting no local symptoms and with a similar temperature curve. In such perplexing cases irregular fluctuation of the fever (the variation between morning and evening being several degrees), the absence of diarrhœa, the presence of dyspnœa with almost negative pulmonary findings, the relatively long duration of the process, its stationary character, hereditary taint, demonstration of tuberculous products in the region of the glands or in the osseous system, and finally the development of the disease after measles or whooping-cough, are suggestive of tuberculosis, whereas enlarged spleen and roseola point to typhoid fever. But even in such cases mistakes are by no means impossible. I, myself, for instance, observed a case in which, immediately succeeding measles, a severe typhoid fever developed. A positive diagnosis of it was made possible only after long hesitation and principally on the basis of its recovery.

It is under just such conditions that the modern bacterial diagnostic methods render valuable aid in enabling us to differentiate between typhoid and tuberculous meningitis. Such differentiation may however be attended with great difficulties at times, cases of abdominal fever occur accompanied by vomiting, scaphoid depression of the abdomen, rigidity of the cervical and dorsal muscles, slow and irregular pulse, "cris céphaliques,"—in short, by all symptoms which point to a tuberculous meningitis, and, on the other hand, a tuberculous meningitis especially in the first years of life, not infrequently exhibits a course like typhoid fever.

In the *agglutination test* devised by Grünbaum, elaborated by Gruber and Pfeiffer in animal experiments, adapted by Widal for clinical purposes, and subsequently essentially improved by Ficker, we possess a method which in the great majority of cases accomplishes the desired object and into the details of which I need not enter. One of the latest tests of the procedure made by Hopfengärtner in children yielded a positive result in all cases examined. The time required for

the observation has been materially shortened by Weil, assistant in the Hygiene Institute of the German University in Prague, in the use of a test, heated to 50° C. (122° F.), half an hour being sufficient to obtain the result. A small apparatus for the typhoid test is furnished by some dealers; this enables the physician to institute a diagnosis conveniently at his own residence.

One objection is the occasional late onset of the reaction, which is rather frequent in children. Under such conditions, a diagnostic examination of the blood may be required, making cultures either from roseola or—what is best in doubtful cases,—from the blood of the brachial vein or the finger tip, according to Castellani's procedure. Jochmann, Flamini, and Rolly report unqualified success by this method in the great majority of cases of typhoid fever in children examined by them, during the very first days of the disease. Finally cultivation of bacteria from the stools may be necessary. According to observations collected by Koch, the method of Drigalski and Conradi will quickly and surely bring about a satisfactory result during childhood.

The **prognosis** is, as a whole, favorable during childhood, although during this period of life grave cases and malignant epidemics may occur. Filatow, a very experienced observer of great clinical acumen, designates as unfavorable prognostic signs fuliginous coating on tongue and teeth, profuse and obstinate diarrhœa, delirium in waking condition (with eyes open), rigidity of cervical and especially dorsal muscles, carphology (picking the bed-clothes with the fingers) thready pulse and other phenomena of cardiac weakness, as well as complete insensibility.

Intense meteorism, too, is a bad symptom, and constantly retracted abdomen with persistently high fever is yet worse.

The **treatment** of typhoid fever, in spite of accurate knowledge of its cause and of its life-peculiarities has as yet not reached any specific method and its principal task lies in adequate prophylaxis—in avoiding the chief sources of infection and as Koch suggests isolating the patients, and carefully disinfecting their surroundings, and morbid excretions. There can be no doubt of the significance of infected water and soil. Sanitation in large cities, consisting on one hand in sewerage and drainage and on the other hand, in supplying wholesome water for drinking, bathing and culinary purposes, has already accomplished remarkable results. Thus, the city of Munich, formerly a notorious haunt of typhoid, has become a salubrious town, and, owing to constant disregard for such sanitary arrangements, Prague has for decades been visited with severe epidemics, against which the individual must protect himself. Individual prophylaxis includes boiling and filtration of water for drinking. cooking, and bathing purposes; cleansing of vegetables, fruit, glasses, etc., with boiled water; avoidance of bathing in creeks or rivers flowing through the afflicted locality whose waters may

contain typhoid bacilli, careful cleansing of the hands of children after they have played in dirt—a series of disagreeable measures after all and still insufficient for protection. Even a close observance of these precautionary directions may at times prove unsuccessful in preventing typhoid fever, for either the lines of defense were not strong enough or other sources of infection, unsuspected, were left open.

In small towns, where the conditions can be more easily surveyed and the course of the disease more closely pursued than in the labyrinthine paths of a metropolis, strict isolation as recommended by Koch must be insisted upon, bacteriological examination of evacuations to be discontinued only when, after repeated observations, freedom from bacilli has been established, strict disinfection of dwelling, etc. Brilliant results have already been attained by following this prophylactic advice.

In private practice, we should isolate the patient and carefully disinfect the stools, urine, and expectorations. This is done best and cheapest by a copious addition of slaked lime to the stools and urine and of a solution of sublimate or a concentrated solution of lysol to the sputa; by subjecting the underclothing and bed clothes to the action of live steam; by keeping the attending nurses away from other patients; by scrupulous cleansing of the hands, etc.

Before dealing with the still necessary symptomatic treatment, I shall briefly review the results of specific therapy. Pfeiffer and Kolle availed themselves of an active immunization method, injecting agar cultures of the typhoid bacillus which had been floated by a solution of common salt and killed by heating. A similar procedure employed by Wright with British soldiers in India is said to have been attended with success. The general harmlessness of this immunizing method, as confirmed on various sides, justifies its trial in severe and widespread typhoid epidemics.

Chantemesse proposed a serum treatment. For this purpose he uses serum from horses immunized by gradually increased injections of a typhoid toxin that he prepared. In patients thus treated he had a mortality of 6 per cent. and it seemed that the process of the disease was milder and shorter. Josias, among 50 cases treated with this serum, recorded only two deaths, and with early injections he produced an abortive course and never experienced any unpleasant after effects. For my own part, I have not yet tested this treatment.

Jez prepares a sort of pulp from the bone marrow, spleen, thymus, brain, and spinal marrow of rabbits highly immunized against typhoid; crushing the pulp in a mortar, and adding a mixture of alcohol, common salt, and water, stirring up the mass, placing it into an ice chest for 24 hours, and finally filtering. The rather clear, reddish yellow filtrate is administered by mouth. In its use, Jez noticed a rapid fall of the tem-

perature and speedy improvement of the symptoms. Results communicated from other sources, however, are contradictory. I used it only once, as prepared in Tavel's laboratory in Berne (Switzerland). The case was a girl eight years old suffering from severe typhoid fever. Two of her younger sisters had the disease but with symptoms less intense. The treatment did not shorten the morbid process, nor influence the temperature curve nor even prevent a relapse. Still, I am not inclined to pronounce judgment on the strength of a single case.

As to *symptomatic treatment*, not much must be expected. I am sure from a rather wide experience in Prague in the treatment of typhoid cases that none of the many antipyretic nor antiseptic methods either in my own practice or in that of others presented anything to convince me of its efficiency. Some of these modes of treatment are disagreeable to the patient, and some distinctly dangerous and for such reasons a wise restriction of their use cannot be too strongly recommended.

The hope of sharply checking the process by energetic primary intestinal disinfection gave rise to the calomel treatment. Apart from the fact that the object in view cannot be attained by any remedy and that for the most part we see the cases at a stage when the blood circulation has already been colonized by the bacilli, the above method is not without certain dangers, as it irritates the bowel and is apt to provoke stomatitis and ulceration of the gums. For the benefit of the patients, it is better not to use it. Whoever wants to use any of the "intestinal antiseptics," as salol, benzonaphthol, etc., will at least not cause any harm. They are administered in the form of a powder or emulsion in daily doses of 0.5–2 Gm. (7½–30 gr.), according to age.

In profuse diarrhœas astringents are indicated. Among these are subnitrate of bismuth, tannalbin, tannigen, fortoin, enterorose, bismutose, ichthalbin, in doses of 0.1–0.25 Gm. (1½–4 gr.), with or without addition of opium, a knife-pointful of these powders three to four times daily. The ordinary typhoid diarrhœa with 2 to 4 evacuations a day is best when unchecked. The strenuous may try to remove a part of the infectious material by the high injections as recommended by Marfan.

Against the fever the whole arsenal of the antipyretic method used to be, and is by many still called into requisition, not for the benefit of the children, but as statistics show at times to their harm, as in collapse from cold baths, or after large doses of antipyretics, and rarely to their joy, as can be inferred from the excitement caused by any of the hydropathic measures in these poor little sufferers. It is my firm conviction gained in the course of many years from the unprejudiced observation of numerous cases, that the progress of abdominal typhoid in childhood is neither shorter, nor milder, nor more pleasant for the children, if the temperature, according to one or another method, is artificially reduced.

The appetite of the little ones is not increased either by the baths or by antipyretics administered internally, but it returns when the fever naturally declines, because the infection has exhausted itself, the body has asserted its mastery, and the toxin which paralysed the digestive functions is formed and absorbed no more.

Above all and most emphatically, I would caution against the strict observance of such antipyretic measures as Brandt's or Vogl's, who have gained for themselves an unenviable remembrance. Such coarse methods (I cannot find a milder designation for them) are apt to produce such disagreeable sensations that the patients do not crave for their repetition.

In case of severe disturbance of the nervous system, especially insomnia, a warm bath—about 35 to 36° C. (95°–97° F.) and given in the presence of the physician—may be serviceable, and if there be any stupor, water of the room temperature may be poured on the head. During the last few years I have, under such conditions when the heart action was good, prescribed small doses of pyramidon, 0.1 to at most 0.15 Gm. (1½ to 2 gr.), administered once in the evening. The reduction of the temperature effected thereby is gradual, but lasting for a long time, and the soothing effect is undeniable.

Other than this I use only hydropathic compresses with slightly heated water, changing them every three hours and covering them with a dry cloth. In case they should give rise to any unpleasant sensations or excite the child I simply dispense with them. Apart from the fact that the little patients generally stand fever very well and often with a temperature of 39° C. (102° F.) and above, will sit upright in their beds and play, they do not feel any better when their bodily temperature has been artificially reduced.

Nutrition is of importance and of course, during the whole period of fever the diet must be liquid and such as milk or in case of dislike of milk, coffee, tea, cocoa, soups, eggs, egg punch (on account of its alcoholic contents indicated when the pulse is small). To increase their nutritive value, somatose, piasmon, tropon, Leube's meat solution, puro, and the like may be added. They should be given in small quantities and at frequent intervals as the patient will not take much—every one and a half, two to three hours—and also abundant drink such as boiled sterilized water, lemonade, light natural acidulated waters, etc.

When there is vomiting or deep stupor makes the taking of food by mouth impossible, enemata may be tried, made of eggs, flour, milk, and salt, or in the form as recommended by A. Schmidt ready for use and sterilized (made by Heyden of Radebeul near Dresden).

Great loss of water as a result of profuse diarrhœa should be equalized by subcutaneous infusions of common salt, and waning heart power strengthened by bold alcoholic administration in the form of mild dessert

wines or champagne, injections of ether, camphor, and the like. Complications involving the lungs require expectorants or inhalations of oxygen and the attempt may be made to check intestinal hæmorrhages by injections of gelatin—two to five per cent., sterilized, in doses of 40 to 80 c.c. ($1\frac{1}{2}$ to 3 oz.) according to age. Intestinal perforation has recently been successfully operated upon by Stewart.

Frequent cleansing of the mouth to prevent or restrict secondary infections is very much to be recommended. This may be done either by washing out the mouth with a piece of gauze dipped in boric acid solution or by repeated rinsing and gargling. Good service is rendered also by menthol vaseline (0.5 to 1 per cent. with vaseline oil) instilled into the nose twice a day.

Scrupulous cleanliness, especially after each evacuation, is the best means for preventing decubitus; also a smooth firm mattress and frequent change of position. There must be an ample supply of fresh air which can best be procured when conditions permit by having two rooms at the patient's disposal which can be alternately ventilated and occupied. If a mixed infection is present it must be treated locally; in case of pus foci, they should be opened and protected by bandages. The appetite may, with the defervescence of the fever, recur with vigor, but its premature gratification by solid food should be sternly refused; the return of the appetite while undeniably welcome is under such conditions rather perplexing. We must make a firm stand against soft-hearted attendants and absolutely forbid all solid food such as soft rolls, meat hash, etc. Such food should be withheld until about a week after complete disappearance of the fever, or even somewhat longer in case the disease has been a severe one. After another week the children, who, in the meanwhile have been out of bed for three to four days, may be allowed out to drive when the weather permits. Where conditions are favorable, a stay in the country during convalescence is to be recommended. Return to school must not be permitted until after complete physical and mental recuperation.

DYSENTERY

BY
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TRANSLATED BY
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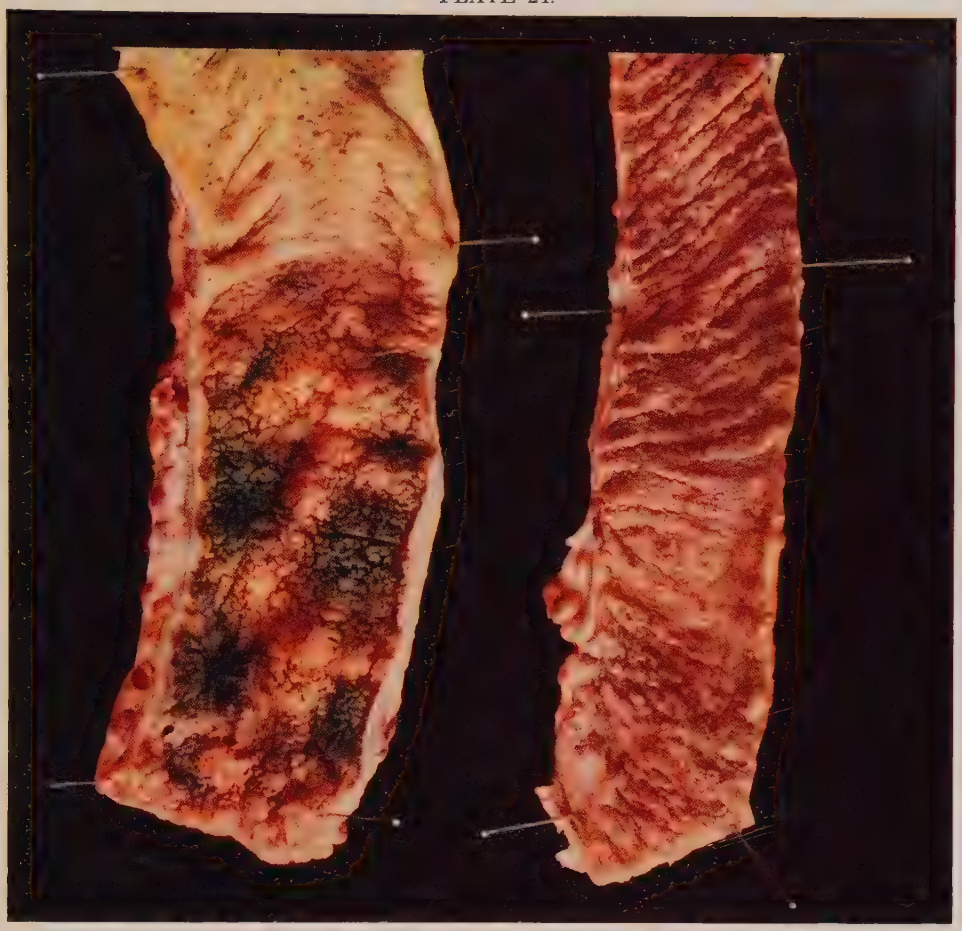
Dysentery is one of the diseases longest known, and may be defined as an infectious disease localized especially in the colon and appearing either endemically or epidemically, the principal clinical symptoms of which are tenesmus, bloody mucus stools, abdominal pain, and early prostration.

Although the clinical picture of the disease has been enlarged by abundant casuistic material, and histological examinations have cleared up the details of the pathologico-anatomical processes in the bowel, yet the etiology was shrouded in obscurity until the last few years. However, recent investigations have resulted in commendable success. Thus it has been established by Kartulis, Lutz, Councilman, and others, that tropical dysentery is caused by a parasitic protozoon, the amœba, and in our latitudes these parasites seem to have an occasional etiological significance, according to Lösch, Alva, Kovacs, Quincke, and others. More frequently, however, the infection is caused by the bacillus of dysentery which has been cultivated from the evacuations by Shiga, Kruse, and Flexner in epidemics of dysentery in various localities. According to the investigations made by these authors, and from a considerable number of later investigations—(the literature bearing on this subject has been carefully reviewed by O. Lentz and Leiner)—there exist several varieties of dysentery bacilli, which may be distinguished from each other not only culturally but particularly by serum diagnosis. Further studies must be undertaken to clear up the question touched by many authors as to the relation of follicular enteritis in childhood to infectious dysentery. Children were the material used as a basis for the observations of Leiner and Jehle.

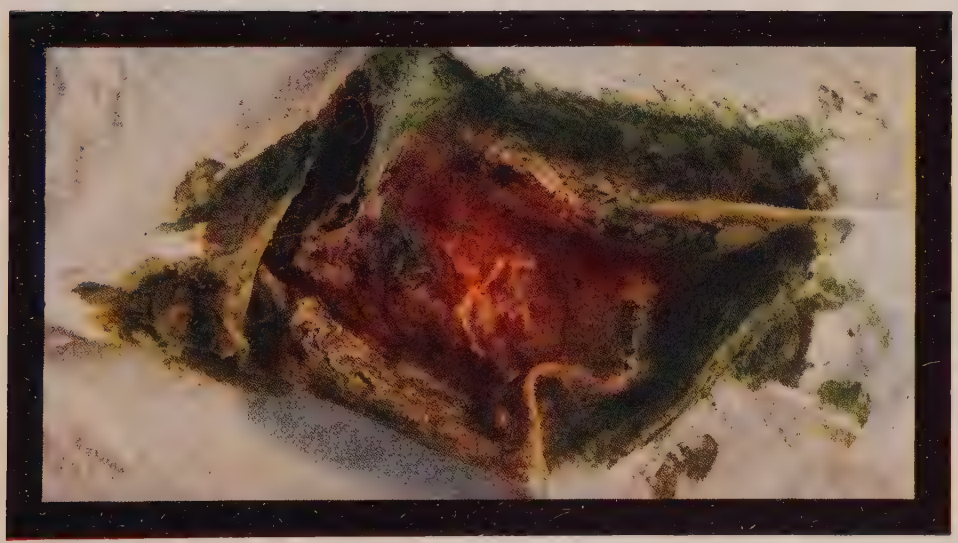
Pathology.—The pathologico-anatomical findings depend upon the intensity of the local process as well as the duration of the disease.

In the mild cases which recover within a few days there are likely to be circumscribed areas of redness and œdema of the mucous membrane of the colon, accompanied by epithelial necrosis, sometimes by shallow ulcerations, while in cases characterized by greater intensity we find flocculent deposits or firmly adherent grayish white or greenish

PLATE 24.



a *b*



c

a. Sigmoid flexure in dysentery (1½-year-old child).
b. Ascending colon in dysentery (same child).
c. Bloody and slimy stool in follicular enteritis (dysentery-like case)(photographed from nature).

yellow membranes on the mucosa, which is strongly injected and œdematous, with here and there hæmorrhagic infiltration. When these deposits and exudates have desquamated, there results an ulceration which varies in size, sometimes isolated, sometimes confluent, or even areas of ulcerations that extend more or less deeply into the intestinal wall and may corrode even the larger blood vessels. The intestinal wall throughout is thickened, œdematous, infiltrated, and the solitary follicles are more or less swollen and their surfaces at times ulcerated (see Plate 24). The serosa over the affected intestine appears dull and lustreless, and the regional mesenteric lymph-glands are swollen and frequently infiltrated with blood. Besides the colon, the cecum and even the lower part of the ileum may become the seat of these pathological alterations. The spleen is usually greatly swollen, while the liver and kidneys are acutely degenerated.

Symptomatology.—The disease, as a rule, begins like an intestinal catarrh, with profuse, diarrhœal evacuations. In one or two days later tenesmus occurs during and after the evacuation. Children affected with the disease, moaning, bearing down and with a painful expression on their faces, usually tarry a long time on the commode and are loath to leave it. The quantity of a single evacuation often amounts only to one or two spoonfuls of at first a glassy mucus, but later on consists of a mucopurulent mass containing small streaks or even small clots of blood, and occasionally dense flocculi or even membranes. The peculiar odor characterizing the early mucus stools is soon displaced by a carrion-like fetor. The latter is due to the putrefaction of extravasated blood, or it may indicate a severe, even gangrenous inflammation of the bowel. The number of evacuations during twenty-four hours fluctuates between 10, 20 or maybe 50 and even more.

The abdomen, for the most part, is depressed, so that on palpation the contracted colon may be frequently felt. In such a case the bowel, either along the whole tract or in circumscribed localities, manifests more or less acute sensitiveness to pressure. The tissue about the anus is usually very much reddened, often excoriated, or even ulcerated, while in the gaping anus may be seen the tensely filled veins and a chaplet-like pad of livid, discolored mucous membrane. The constitutional symptoms soon become manifest. The colicky pains that precede and accompany the evacuations with the consequent tenesmus torment the patient not less than the intense thirst. The sufferer is deprived of sleep, or sleeps only lightly. Even a few days after the disease has set in the patient's face exhibits a painful expression, the eyes are circled with blue, the lips are usually dry and fissured, the tongue dry and thickly coated, the appetite is gone, and often there exist nausea and vomiting.

It is distinctly characteristic of dysentery that within a few days

the skin becomes very pale and there is a rapid loss of strength and great emaciation. The urine is usually lessened in amount and may contain albumin and casts. The temperature presents nothing characteristic. It may be normal or subnormal, but in the majority of cases it exhibits an irregular remittent type.

In a microscopical examination of the stools we find, in and around the structureless mass of mucus, intestinal epithelia, single and grouped leucocytes, which are usually polynuclear; erythrocytes normally colored or shadowed, often agglutinated, the occasional remnants of vegetable or animal food and remarkably few bacteria. Concerning the bacteria it may be stated that in a cover-glass preparation the presence of a few short, plump, free or endocellular bacilli, negative to Gram's stain with many pus corpuscles may strengthen our suspicion as to an infection by dysentery bacilli. But a further identification of the latter is possible only by means of cultures or finally by serum diagnosis.

The **progress** and **termination** of dysentery vary, a complete return to health in a majority of the cases ensuing in a more or less short (1 to 2 weeks) or long time (3 to 4 weeks). But the convalescence of the patients may, without any manifest cause be interrupted by one or more relapses. Cases which are grave or very severe from the outset may terminate fatally within a few days, owing to a collapse or various complications. Signs of favorable trend are remission of tenesmus, the occurrence of stools of a feculent odor and of flatus, decrease of thirst, refreshing sleep, and return of the appetite.

Cases continuing for several weeks or several months, in which periods of improvement and apparent cure alternate with relapses, are usually designated as chronic dysentery. Not infrequently such cases occasion a severe marasmus or certain sequelæ or complications may lead to death.

The following **complications** of dysentery have been observed: Severe thrush, stomatitis either aphthous or ulcerative, noma, suppurative parotitis, icterus, liver abscesses, peritonitis, fissures of the anus, prolapse of the anus and rectum, gangrene of the prolapsed anus, bronchitis, bronchopneumonia, pneumonia, atelectasis, pleuritis, pyæmia, obstinate tendinous and articular inflammations.

As **sequelæ** there have been recorded: chronic colitis, membranous enteritis, stricture of the anus, of the rectum and of the colon, disturbance of the nerves of the lower extremities, anæmia and marasmus.

The **diagnosis** in a majority of cases of infectious dysentery is easy; the intestinal symptoms and the examination of the stools, especially in an endemic or an epidemic of the disease, being sufficient. More difficult, however, is the etiological diagnosis of a sporadic case, as well as the differential diagnosis of severe cases of follicular enteritis which may be caused by infection with highly virulent colon bacteria (Rossi-

Doria, 1892, Escherich, 1895, Finkelstein, 1896). In such contingencies an exact etiological diagnosis is possible only by means of culture and serum reaction.

The **prognosis** depends on the intensity and extent of the local process, the complications, and the constitution of the patient. The mortality in several epidemics has fluctuated between five and thirty per cent.

With regard to the **prophylaxis,** the cases of dysentery must be isolated both in private practice and in the hospitals, the evacuations must be disinfected, and the attendants, both for their own interest and that of those around them, must be scrupulously clean.

Treatment.—As to the treatment, the dysentery patient should be confined to bed, even if the disease be only light. Warm compresses, in moist or dry form, applied to the abdomen, are appreciated by most sufferers. The diet should consist of mucilaginous soups made of oatmeal or flour, and later on may be given gradually, milk, gruel soups, eggs, purées, and minced meat. To relieve thirst, tepid tea, coffee, pure water, or sugared water to which some brandy or a few spoonfuls of red wine have been added, are advisable. In weakness or collapse cognac or medicinal wines (Mavrodaphne, St. Maura, Sherry, etc.) in large doses, should be administered, and injections of camphor in oil (camphor 1 part in 9 parts of olive oil) may be given several times a day, ½–1 c.c. (♏ 7½–15) with a Pravaz syringe. For the same purpose a subcutaneous injection of 150 to 250 c.c. (5 to 8 oz.) of 0.8 per cent. solution of chloride of sodium can be recommended.

After each bowel movement, the anus and the adjoining parts should be cleansed with water, and then powdered or coated with vaseline. Medicinal treatment should, whenever possible, begin with an evacuation of the bowels. For this purpose the salines or castor oil is given; of the latter, according to the child's age, a teaspoonful or tablespoonful is given every half hour or hour, until a stool follows and the oil appears in the excreta. As castor oil is thick and viscous, the spoon should be heated over a candle. The following emulsion is a favorite:

℞ Olei ricini ..... 10–15–25 ..... ʒ ii–ʒ vi
Ad emulsionem spl. ..... 90 ..... ℥ iii
Glycerini ..... 5 ..... ʒ i
Sig.—A teaspoonful to tablespoonful every half hour or hour until desired result is obtained.

Calomel is apt to provoke tenesmus or increase enormously that already existing and cannot be recommended for dysentery.

Tenesmus may frequently be alleviated by warm compresses applied to the perineum, or by an enema of 20 to 50 c.c. of water of the same temperature as the body 2 to 3 times a day, or an amylaceous decoction (1 teaspoonful of starch to 1 litre of water), with later addi-

tion of tincture of opium—one drop for a two-year-old child; two drops for a three-year-old; three drops for a four-year-old, etc., in the 24 hours.

Often suppositories have to be resorted to and may be introduced twice a day. As anæsthetics may be recommended opium or anæsthesin, the latter in doses twice as large as the former.

℞ Extr. opii aquosi 0.005.....$\frac{1}{12}$ gr. .....for two-year-old child.
0.01.....$\frac{1}{6}$ gr. .....for three-year-old child.
0.02.....$\frac{1}{3}$ gr. .....for five to six-year-old child.
Butyri cacao q. s. ut. fiat supp. minus.
Dentur talia suppos. No. IV.
Sig.—Introduce one or two daily.

Local cold applications are also serviceable. One may introduce into the anus a piece of pure ice of the size of a cherry every 5 to 10 minutes for half an hour to one hour.

After the cleaning of the bowel one may give internally subnitrate of bismuth several times a day. For instance, every three hours:

0.1.....gr. iss.....for a child half a year old.
0.2.....gr. iii.....for a child one year old.
0.3.....gr. ivss.....for a child two years old.
0.4.....gr. vi.....for a child three years old, etc.

The bismuth may be given also in emulsion, to be well shaken before taking.

℞ Bismuthi subnitr.... 0.5.....gr. viiss.....for child one-half year old.
Aquæ destillatæ ....70.....f℥ii ℥iiss.
Mucil. gum. arab....20.....℥v.
Syr. spl.....10.....℥iiss.
Sig.—A teaspoonful every three hours. Shake well.

Instead of the bismuth salt, the bismuth albumin combination, bismutose, may be given in doses about three times as large.

As internal astringents, tannalbin or tannigen may be used three to four times daily, in doses of 0.3 to 0.5 Gm. ($4\frac{1}{2}$–$7\frac{1}{2}$ gr.). Their combination with doses of bismuth corresponding to the age of the child is quite beneficial. In persistent fever tannate of quinine renders good service. Give three to four times a day:

0.03 to 0.05.....gr. ss–i.....to a child one-half year old.
0.1.....gr. iss .....to a child one year old.
0.15.....gr. ii.....to a child two years old.
0.2.....gr. iii .....to a child three years old.
0.25.....gr. iv .....to a child four to five years old.

Local treatment of the intestinal process with irrigations, although appearing theoretically advantageous, proves usually too irritating at the initial stage of the disease and must therefore be reserved for a later period. One may use enemata containing $\frac{1}{2}$ to 1 per cent. of table salt

and the cleansing injection may be followed by the introduction of an astringent, the quantity of which must never exceed 150 to 200 c.c. The astringents used are:

0.5 to 1 per cent. solution of tannic acid.
1 to 2 per cent. solution of liquor aluminum acetate.
0.1 per cent. solution of nitrate of silver.

The last mentioned should always be followed by a second irrigation with a weak solution of common salt. They should be made daily or every other day. In protracted cases I have found efficacious the injection daily or every other day of an emulsion of bismuth in a mucilaginous vehicle.

1 to 2.....gr. xv–xxx.....subnitrate of bismuth for children two to three years.
3 to 4.....gr. xlv–ʒi.....subnitrate of bismuth for children four to five years.
5 to 8.....gr. ʒi–ii.....subnitrate of bismuth for children over five years.

Given in 100 Gm. (3 oz.) mucilage, gum arabic, etc. But such an enema should always be preceded by a cleansing injection. Complications and sequelæ that were previously mentioned require an individual symptomatic treatment.

Further observations are needed before the specific serum therapy of dysentery as established through animal experimentation by Kruse, Shiga, Rosenthal and Kanel and already clinically tested, can be introduced into general practice. It is only quite recently that, Lüdke has affirmed the favorable effect produced by Kruse's dysentery serum.

INFLUENZA

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TRANSLATED BY
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INFLUENZA has the same importance in childhood as in adult life and it is worthy of special study because it exhibits a number of characteristic and important modifications.

Influenza is known to have been prevalent in the fourteenth century, but a clinical and scientific knowledge of the disease was not obtained until the epidemics of 1830 and 1840. A great advance in our knowledge of the disease was made during the great pandemic of 1889 to 1891.

Influenza (epidemic grippe) is an acute contagious and infectious disease occurring mostly in epidemics and its cause is a specific organism, the bacillus of influenza.

R. Pfeiffer discovered this bacillus in 1889 after a number of false observations had been published. His work has been verified by repeated investigations so that to-day the importance of Pfeiffer's bacillus of influenza is no longer in question. It is a small, rod-shaped bacillus, strongly anaërobic, with very slight resistive power and short-lived outside the body. Its vitality is soon destroyed in water and in earth, and for cultivation it must be grown on blood hæmoglobin at a temperature between 26°–43° C. (76°–106° F.). The contagion is spread from the secretions of the mucous membranes. The bacillus is found in vast numbers in the nasal secretions, while in an ordinary coryza very few bacilli are present. At first the bacilli are found free in the secretion, but later inside the pus cells. For a rapid bacteriological diagnosis it is best to make smears from the nasal secretion and stain with a weak carbol-fuchsin solution. In children the bacillus has been found in the blood, various secretions, cerebrospinal fluid, in pus from the ears, etc.

The *incubation* period differs according to different authorities from one to eight days.

The many variations in the clinical picture of this disease are due to the fact that there is an infectious inflammation of dissimilar organs and tissues.

The parts most affected are the respiratory mucous membranes, through which the bacillus gains entrance into the system, the alimentary tract, and the nervous system as a result of toxic irritation.

The predominance of various symptoms depends on the part specially affected. The symptoms may be loosely grouped into those of catarrhal, gastric and nervous (rheumatoid) influenza and at times into a combination of all three.

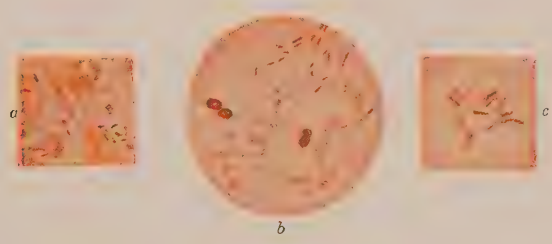
In a widespread epidemic no age escapes, although it is comparatively rare in early infancy. It occurs most frequently from fifteen to forty years of age. The ages of 47,000 cases treated by physicians in Bavaria in 1889 and 1890 were as follows:

Age.	Per cent.	Age.	Per cent.
1	1.5	16–20	11.4
2–5	5.4	21–30	22.2
6–10	6.6	31–40	19.3
11–15	7.2	41–50	12.6

Epstein's statistics show 1.6 per cent. in the first year, 12.5 per cent. from one to ten years, and $36\frac{1}{3}$ per cent. from ten to twenty years. Strassmann has reported cases occurring in the newborn.

The *source of infection* in the newborn and young infants is the

FIG. 107.



Influenza bacilli. (*a*) In nasal secretion; (*b*) in culture with bacillus sputigenes crassus; (*c*) diphtheria bacilli for comparison.

mother, yet nursing babies acquire a relative immunity through the mother's milk as is observed in other infectious diseases.

The younger the child the more marked are the intestinal symptoms, with secondary involvement of the central nervous system, which gives it more the nature of a general infection or intoxication. The symptoms on the part of the respiratory apparatus become more pronounced as the child grows older.

The *onset* of the disease is usually sudden. Children first complain of feeling tired and indisposed and on examination appear depressed and listless, complain of headache and show some fever. There is a marked distaste for food; the facial expression is anxious; cyanosis is frequent; the eyes are watery and sensitive to light; and herpes corneæ is not uncommon. The pulse is rapid and there is tenderness of the neck, back and legs. The younger the child, the more indistinct is the clinical picture. In very young children the disease may be ushered in by vomiting and convulsions and other symptoms of meningeal irrita-

tion, also intestinal disturbance, constipation, diarrhœa, coryza and a dry, hacking cough.

The above brief sketch of the disease must be described in detail.

The **temperature** rises rapidly with the outset of the disease to 40°–41° C. (104°–105° F.), and in uncomplicated cases subsides to normal in 24 to 48 hours. In rare cases it terminates by lysis and may resemble the typhoid curve. A condition of collapse, with a temperature of 30° C. (90° F.) or less, may occur in infants and children with meningeal symptoms.

Headache generally accompanies the fever and is referred by older children to the frontal region, less often to the temporal. The supra-orbital region and the eyes are very sensitive to pressure due to cerebral congestion. The headache is very severe.

The *pulse* shows nothing typical of the severity of the disease. It is small, compressible, arrhythmic and of varying frequency.

The striking exhaustion and subjective lassitude as well as the general hyperæsthesia are symptoms present in children equally with adults. The tenderness becomes apparent in young children when attempts are made to lift or move them.

Examination of the buccal cavity and pharynx of a fresh case shows a diffuse and characteristic congestion of the parts. Soltmann in 1887 described the appearance as follows: "Influenza in children does not begin with a nasal catarrh but with a retropharyngitis."

As a number of diseases in children are characterized by a hyperæmia of this region it is necessary to describe the diagnostic features. The congestion is sharply defined from the unaffected tissue. Redness and cyanosis frequently appear in lines along the surface of the pharynx and later a fibrinous exudate is formed which strips off. The entry into the system occurs through the pharynx.

The influenza infection may first show itself in older children as in adults, with a *coryza* having a scant, thin secretion. A dry bronchitis with a paroxysmal cough may follow this. The younger the child the less pronounced are the respiratory symptoms.

In Schlossmann's cases under three years, 35 per cent. showed no or only slight broncho or pulmonary involvement at the beginning of the disease, while in cases over ten years of age, five-sixths began in this manner.

The coryza is accompanied by a severe congestion of the nasal mucous membrane which often produces nosebleed.

The *cough* is dry, severe and racking and similar to that in the prodromal stages of measles, and may simulate the paroxysm of pertussis. Some authors speak of a "pseudopertussis" in the course of influenza. This irritative cough often continues during the period of convalescence. The termination of the congestive catarrh is in all cases rather late and the discharge may finally become mucopurulent.

In certain epidemics a severe and dangerous membranous croup or pseudocroup has been reported. Concetti describes this as the "forma laryningea" of influenza.

Complications on the part of the *respiratory system* unfortunately are not uncommon. Bronchopneumonia appears in its characteristic way in older children, but in very young or weak infants it may run a latent course and terminate suddenly in a fatal outcome. Lobar pneumonia occurs rarely but in an outspoken manner, as in childhood. The typical influenza pneumonia so thoroughly described by Finkler appears only rarely in children. Whether the pneumonia is a specific symptom of the disease or a secondary infection on a fertile and predisposed ground is an academic question. The course of the disease as well as the severe systemic toxæmia stamps this as a very serious complication. Pleurisy is not uncommon and Meunier found a serous effusion in ten out of eleven cases.

In the early years of life all affections of the respiratory organs have a less menacing character than in later years. The danger of a secondary tuberculous infection is less than after measles or pertussis.

The congested condition of the mucous membranes of the mouth and throat is participated in by the conjunctivæ. Conjunctivitis with photophobia is of frequent occurrence and reminds one of the prodromal symptoms of measles. In small children the inflammation may extend into a blepharitis ciliaris and a resulting spasm of the lids. A superficial keratitis and herpes corneæ have been observed. Dakryocystitis may follow by extension from the nasal mucous membrane.

The *ear* is involved by a direct extension of the inflammation from the pharynx through the Eustachian tube. Nearly every child suffering from influenza complains of more or less severe earache. Often this is simply a neuralgic otalgia. Inflammation of the external auditory canal may occur. On inspection in most cases a dark opaque redness of the drum membrane is seen, while in the severe cases either small or large hæmorrhages may be detected. This hæmorrhagic middle ear inflammation may develop into a purulent otitis media. When this occurs there is bulging of the drum, a secondary rise in temperature, and severe pain. Relief is immediate after paracentesis, and influenza bacilli may be detected in the discharge. Three-fourths of all cases are unilateral. Mastoiditis is not an uncommon termination. Exceptionally there may be severe labyrinth disease (Habermann had a case in a two-year-old child).

Influenza is often accompanied by a severe and painful tonsillitis which may become follicular and covered with an exudate.

Gastro-intestinal symptoms were not formerly regarded as a part of the clinical picture of influenza. The earlier writers regarded influenza only as an infectious catarrh of the upper air-passages. Now the diges-

tive apparatus plays an important part in young children and infants and in many cases the whole course of the disease may simulate an acute febrile gastro-intestinal catarrh.

In adults we find loss of appetite, vomiting and diarrhœa as prodromal symptoms. The younger the patient the more marked are these symptoms. Dyspepsia of varying severity is present in nearly all cases in children. The anorexia, coated tongue, and vomiting are suspicious of meningeal irritation. A transient constipation followed in a few days by diarrhœa is quite common. The stools are fetid, become more frequent and fluid and together with the other symptoms, marked prostration is produced. These intestinal symptoms may become so severe as to simulate typhoid fever.

The intestinal symptoms, which are an extension of the inflammatory process, prepare these parts for the development of secondary infections and the resulting systemic toxæmia.

Enlargement of the spleen is irregular in influenza and is never marked.

Albuminuria occurs in from six to ten per cent. of children suffering from influenza. An acute nephritis may develop similar to that in scarlet fever, and cases of the acute hæmorrhagic type have been reported. A case of secondary pyelitis following influenza has been observed. Anuria may occur due to a paralysis of the bladder muscles (*m. detrusor*) resulting from the effect of the toxin on the nervous system.

The effect of the toxæmia is especially noticeable in the involvement of the *heart.* In the early stages of the disease this is shown by arrhythmia and tachycardia. Later on the heart action becomes slower and there is a slight dilation with indistinct murmurs. This may result in cyanosis and collapse. The toxæmia shows a close similarity to that of diphtheria in its effect upon the innervation of the heart and in the parenchymatous degeneration of the heart muscle.

This relative heart weakness must be borne in mind for a long time in severe cases. True and even severe endocarditis has been observed after influenza.

The third group of symptoms—*nervous influenza*—are found in all well-marked cases. The severe depression, the aching bones, the weariness, the pain in the limbs and muscles, and the sensitiveness of the spine are all included in the term nervous or rheumatoid influenza. Localized peripheral nerve tenderness is frequent; but true, long-continued neuralgias are uncommon in children.

Of much greater importance is the involvement of the brain and its membranes. A diagnosis from diseases of the meninges is uncertain in the beginning of an infectious disease with high fever as in influenza.

Meningeal irritation or meningismus occurs easier and much oftener

in young children. From this to severe inflammation of the meninges we find all degrees of involvement diminishing in intensity with age.

These symptoms are usually due to the toxin except in the fortunately rare cases where there is an exudative, purulent, or parenchymatous change in the meninges. This toxic irritation is the cause of the severe headaches with the exception of the congestions, the eclamptic seizures and the various irritative symptoms (laryngospasmus) so easily developed on the unripe nervous system of the child. In young children where the entire family is affected, a stuporous condition is often present alternating with eclamptic seizures. A slight opacity of the meninges was the only post-mortem finding in two such fatal cases.

True meningitis as a result of the infection is either due to the influenza bacillus or is secondary to a secondary infection from the middle ear.

The bacillus of influenza has frequently been found in the meninges and has been obtained by lumbar puncture in the living.

Hæmorrhagic encephalitis and acute poliomyelitis have been observed after influenza and severe degenerative changes as in sclerosis have been described.

Psychoses of a more or less severe grade are occasionally seen during convalescence. These are manifested by hallucinations, cataleptic stupor, etc. The mind generally returns to its normal condition after strength has been restored. The disease may be ushered in by mental confusion, as in Ewald's case of a seven-year-old boy who at the outset of the disease went to the railroad station and boarded a train instead of going to school, without any recollection of what he was doing. Many children at the beginning of the disease fall almost in a condition of lethargy for which there is no satisfactory explanation. Heubner also found it during convalescence. Acute dizziness and delirium when present are a result of the high toxic fever.

In most cases of influenza there are no changes in the skin. However, it is not at all uncommon to find an *exanthem* in the course of this disease upon which too little emphasis has been placed. Generally this is a small, punctate, confluent erythema with itching which is found on the chest, abdomen and sides of the extremities. The exanthem in the majority of cases is very similar to that of scarlet fever and this may render the diagnosis under certain conditions exceedingly difficult.

Other eruptions may appear after a few days or in the second week. Filatow and others have described an eruption similar to measles and cases resembling urticaria, roseola, and purpura have been described.

It is doubtful if these rashes are a result of a mixed infection with influenza. In a large number of exanthemic infectious diseases the influenza bacillus has been found in the blood and different organs. A mixed infection with diphtheria has been reported and Jochmann found

the influenza bacillus in a case of pertussis. Many authors have found the influenza bacillus to be the cause of a pneumonia occurring in the course of other diseases.

The lymphatic system plays a small part in influenza.

An uncomplicated case of influenza is generally only of a few days duration but it may be prolonged several weeks. The various complications make the course of the disease very uncertain. This is especially true when the lungs are involved and a chronic congestion results which is very slow in disappearing. Filatow and others have described a protracted form of influenza which may persist for months without any special catarrhal manifestations, but showing a mild degree of fever, headache and weakness. The possibility of tuberculosis must not be overlooked.

The **prognosis** of uncomplicated influenza in children is favorable even when the lungs are involved but it should be guarded when the heart is affected. In general the prognosis depends upon the symptomatology of the individual case. An influenza grafted on an existing tuberculosis is very unfavorable.

The **diagnosis** of influenza in children is not always simple when there is no epidemic, but when whole districts are affected it is a very easy matter. At such times the possibility of other diseases with symptoms similar to influenza should be borne in mind. After the exclusion of other diseases, the symptom-complex on the part of the various organs, the height of the fever and extreme weakness, the typical appearance of the mouth and throat all tend to establish the diagnosis.

Unfortunately the bacteriological diagnosis is seldom available for practical purposes. It is difficult to make the diagnosis when the symptoms described as meningismus are present. Have we to deal with a beginning influenza, or some form of true meningitis? In influenza we may find some retraction of the head with tenderness on motion and irregular pulse and respiration. Rapidity and arrhythmia of the pulse are characteristic of influenza when it is present. Lumbar puncture in these cases is of the greatest diagnostic importance.

In the *differential diagnosis* several possibilities must be borne in mind. Influenza with sore throat and a scarlatiform rash may simulate scarlet fever but the course of the fever and rapid disappearance of the rash will suffice in most cases to clear the diagnosis. Desquamation and infection of the lymphatic nodes never occur in influenza.

In measles there is a longer prodromal period, the rash reaches its height in three to four days, the presence of Koplik's spots, the severe conjunctivitis, the sneezing, etc., all speak against influenza. Typhoid is recognized by the enlarged spleen, roseola, and diazo and Widal reactions. The possibility of miliary tuberculosis may come in question for a few days.

The **pathology** of influenza has nothing distinctive. There may be the characteristic appearance of pulmonary complications with small areas of consolidation which, deeply congested or hæmorrhagic, are about the yellow stained bronchi and separated by rather firm round-cell infiltration of the connective tissue. Abscess and necrosis of the lung are not uncommon.

There are no distinctive changes in the spleen, heart, liver and kidneys except that the influenza bacillus can be cultivated from them. The other changes such as inflammation of the gastric mucous membrane are purely symptomatic.

The **prophylaxis** depends upon avoidance of cold and exposure and removal from a locality or school where influenza is epidemic. Children at such times should be kept away from crowds, meetings, and public conveyances.

The **treatment** is in a great measure purely symptomatic. The management of complications such as pneumonia, otitis, meningitis, etc., is described in detail in other chapters.

The child must be kept in bed. The diet should be generous, not a starvation diet, but one rich in carbohydrates, poor in proteids and preferably fluid at first. Nursing infants should not be taken away from the breast. Older children take with benefit copious amounts of water, lemonade, fruit juices, etc. Hydrotherapy is of great advantage especially in young children. Cold packs with lukewarm baths and rubbing are helpful. Heubner advises placing the child in a warm bath and pouring cold water on the chest to overcome the intense stupor in some cases. Cold baths should be employed to reduce the fever.

There are no specific drugs in influenza. The salicylate of quinine in small doses is of benefit. Aspirin and the benzoate of soda are useful in older children. The benzoate of soda is both antiseptic and antipyretic and has no unfavorable after-effects. Inhalation of the tincture of benzoin is very soothing to the inflamed mucous membrane. For the bronchitis and diarrhœa small doses of tinctura opii benzoica are useful. Antineuralgic drugs may be employed to ease the earache.

WHOOPING-COUGH

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TRANSLATED BY
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HISTORICALLY, whooping-cough may be regarded as a recent disease. The first description of a whooping-cough epidemic we owe to DeBaillou (1578) and in the seventeenth century Willis, Sydenham, and others recognized the disease and differentiated it from those symptomatologically related to it. Whooping-cough has since become an affection common to all latitudes, with a tendency to assume every year in unequal waves an epidemic character. The frequency of epidemics and the opportunity that has existed daily for decades and centuries, to observe the disease; its symptoms, recognizable even by a layman, and the fact that for the purpose of establishing a diagnosis even the recent finer methods of examination may be dispensed with,—all these factors have contributed towards advancing the symptomatology and diagnosis of whooping-cough (Biermer, Barthez and Rilliet, Hagenbach, Sticker), whereas its pathogenesis and etiology are still under discussion, in spite of laborious investigations made with modern equipment.

Whooping-cough is a contagious infectious disease. The primary symptoms involving the respiratory tract, the transmission of the disease through the sputa, and the usually afebrile course in uncomplicated cases might be regarded as criteria of a *local* infectious disease. But the occurrence of an initial fever wave, which close observation reveals, and which does not run parallel with the respiratory signs, an early inflammatory leucocytosis, the similarity of the initial symptoms to those of other general affections, the permanent immunity almost always acquired by those who have had an attack of pertussis, the course and mechanism of the attacks of coughing differing from other conditions of local irritation of the respiratory mucous membrane, and finally certain complications that probably can be accounted for by the action of toxins, justify one in considering whooping-cough as a general infectious disease whose portal of entry and principal symptoms are found in the respiratory tract.

The *transmission* of the disease from the sick to the well is usually direct and immediate, in a great majority of cases, through the sputum scattered by coughing. A mediate, indirect infection through sputum

adhering to clothes, handkerchiefs, playthings, benches, etc., is very rarely met with. The virulency of the sputa, that is to say, the durability of the exciting cause, lasts only a short time.

The susceptibility to whooping-cough varies especially with the age of individuals exposed to the danger of infection. Statistics proving the enormous prevalence of pertussis in children justify the designation of whooping-cough as a disease of childhood. Those who have reached the age of puberty are far less susceptible to pertussis than to other acute infectious diseases occurring chiefly in childhood.

A collection of the cases of whooping-cough reported in the city of Vienna, in 1899, 1900 and 1901 as published in the statistical yearbooks, shows:

In the first year of life	1242 cases.
From the second to the fifth	3139 cases.
From the sixth to the tenth	1926 cases.
From the eleventh to the fifteenth	135 cases.
From the sixteenth to the twentieth	12 cases.
From the twenty-first to the twenty-fifth	2 cases.
Beyond the twenty-sixth year	13 cases.

The *age* before compulsory school attendance is most affected. The susceptibility shared by all children makes every case imported into the family from the school, the nursery, the kindergarten or the public playground a starting-point for a house epidemic likely to attack the youngest of children. The first year of life, as seen from the above statistics, is less often involved than the following, but nevertheless it is to a considerable extent even more than by measles. Whether this is due to a certain lowered susceptibility or to the less frequent contact with other children, especially in cases of first-born, cannot be certainly decided. But that the first few days or weeks of infantile life do not mean immunity from whooping-cough, may be proven by many closely observed cases. Bouchut reports a case in which a newborn child, infected on the second day, began to cough on the fourth day, and on the eighth day had pronounced paroxysms of whooping-cough. Rilliet and Barthez reported a case of pertussis in a newborn child whose mother had whooping-cough. Watson observed whooping-cough on the first day of life, and I know of a case in a child fourteen days old. Porak and Durante, during a local epidemic at the Paris Maternité noticed a lesser disposition to whooping-cough in the prematurely born (10 cases out of 44), but a greater susceptibility in those born at term, mostly fed by different wet-nurses (10 cases out of 14), all these infants being less than one year old. At the other extreme of life, cases of whooping-cough are known to have occurred during old age.

All observations made on an extensive scale show that the female *sex* is the more largely involved. From 1899 to 1901, 6666 girls as

against 5127 boys were officially recorded in Vienna as having been affected with whooping-cough.

While in large cities pertussis never disappears entirely and the preponderating involvement of the first years of life in the morbidity of whooping-cough may be regarded as the expression of a general susceptibility of man, to which even the very youngest are subject, remote countries, cut off from the outside world (*e.g.* the Faroë Islands), are apt to become rapidly infected from a single exposure and to suffer a general dissemination of the disease. The immunity acquired by a large percentage of persons who early in life have had an attack, as well as a certain reduction of their susceptibility, affords a protection to adults.

Attempts made in various quarters from observations extending over decades to determine a certain periodicity for the epidemics of whooping-cough have not led to any satisfactory conclusions. Neither season nor weather nor other conditions such as the increased contact of children at the beginning of school, appear to occasion an epidemic-like expansion of the morbidity curves.

Figures arranged according to months showing the number of cases of whooping-cough officially recorded in Vienna during five years (1898 to 1902) exhibit the highest number for March (1332) and April (1243), the lowest for October (555). Other observers, however, report differently.

It seems that the raw periods of the year more frequently cause an increase in the morbidity figures and a protracted duration of single epidemics, corresponding to the deleterious influence exercised by inclement weather in general on affections of the respiratory tract. The alternation of measles and whooping-cough epidemics, sometimes observed but often overestimated as to its frequency, may possibly be accounted for in a similar manner. In both infectious diseases a distinct involvement of the respiratory tract is a prominent feature; in both, the portal of entrance of the pathogenic factor is presumed to be in the mucous membrane of the respiratory tract. Thus a catarrh accompanying one of these diseases might easily facilitate an infection with the other.

Since the disease has been completely described symptomatically, attempts based on anatomical and clinical experience have been made to investigate the *etiology* and *pathogenesis* of whooping-cough. The favorable prognosis of uncomplicated cases prevents obtaining post-mortem findings undoubtedly underlying the basal disease. After death, we find almost always lobular-pneumonia and tuberculous alterations of the lungs and lymph-nodes, together with evidences of pulmonary emphysema, dilatation and hypertrophy of the heart, changes in the central nervous system (see nervous complications) capillary hæmorrhages, etc., according to the clinical complications. The ever-present catarrh

of the respiratory mucous membrane and its localization as may be determined laryngoscopically during life should support the theory that whooping-cough is a specific catarrh causing because of its localization, a spasmodic cough. However, laryngoscopic findings, credited almost exclusively to older investigators, differ quite considerably, both with regard to the intensity and especially the localization of the alterations. But it seems that the rima glottidis posterior is the point of irritation at which the tenacious little lumps of sputum, rich in mucin, driven up from the deeper bronchial branches by the movements of ciliated epithelium, excite the paroxysm.

Against the conception of whooping-cough as a specific laryngotracheitis, the following facts have been justly brought forward: the rhythmic process of each paroxysm and of the whole affection differing from such catarrhs, the influence exercised on the symptoms by the state of mind, the convulsion phenomena during and between the individual attacks, and finally the frequent inactivity of narcotics, especially in the catarrhal stage. These facts were more apt to cause whooping-cough to be numbered among the functional nervous diseases. But its acute onset and undoubted contagiousness as shown by everyday observations make the inclusion of pertussis among the contagious infectious diseases the only justifiable one.

The *transmission* of whooping-cough from an infected to a healthy individual naturally led to the assumption that the pathogenic virus was to be looked for in the sputum and the mechanism of the process in the infection by aspiration of little drops of infectious expectorated matter. There are two possibilities to consider: whooping-cough may be regarded either as a local infectious disease of the respiratory tract, the irritant being produced in the larynx or trachea, and (contrary to most other infectious local diseases) by reaction of their toxic products established a permanent immunity in those who had once been affected; or it may be considered as a general infectious disease which, starting primarily from the mucous membrane of the respiratory tract, produces the clinical symptoms through toxic products. As already stated, a number of weighty facts speak for its acceptance as a general infectious disease.

The *exciting factors* of whooping-cough have been searched for throughout many decades, since Linnæus, and the results obtained time and again, seemingly successful, have brought forward organisms of the greatest biological variety. Deichler, Kurloff, and Behla thought protozoa were the cause of pertussis, while Moncorvo and Silva-Aranja, Broadbent, Haushalter, Mircoli, Ritter, and others regarded cocci as the pathogenic factors; Burger, Afanassiew, Szemetschenko, Wendt, and Genser considered bacilli as the causative agents. Quite recently Czaplewski and Hensel on one hand, Jochmann and Krause on the other,

and finally Manicatide have described certain bacilli which may bring us nearer to a bacteriological knowledge of whooping-cough.

Czaplewski and Hensel found in the expectorations, after staining with carbol-glycerin-fuchsin and treating the preparations with 1 per cent. acetic acid, many small short bacilli with rounded corners, about the size of an influenza bacillus, but differing from the latter in that they grow on ordinary culture media. The bacilli are two to three times as long as broad. If delicately prepared, polar staining is shown; while if strongly stained, total staining is accomplished. Experiments on animals proved negative, but their regular occurrence, according to the authors, is suggestive of specificity. Cavasse, Wagner, von Zusch, Koplik, Arnheim, and Reyher were able on the whole, to confirm the findings (see Fig. 108).

Jochmann and Krause, in their investigations made at the Hamburg-Eppendorf hospital, found in whooping-cough sputa in a majority of cases tiny, influenza-like bacilli of morphological identity. However, these they say, do not belong to one species, but represent three different ones distinguished from each other biologically, for example by their behavior towards Gram's method of staining. The influenza-like bacillus found by Czaplewski and Hensel was detected by Jochmann and Krause in only four cases. The latter claim as the cause of whooping-cough an influenza like Gram-negative bacillus (*Bacillus pertussis* Eppendorf), growing only on culture media containing hæmoglobin. They found this organism in eighteen cases.

A third type of bacillus resembling those of influenza, growing in all ordinary culture media and being Gram-positive (bacillus z), was found by Manicatide. Its specificity he claims to have established by serotherapeutic experiments, immunizing three sheep and two horses and, by injection of the serum, effecting a cure or at least an improvement in positive whooping-cough cases.

The bacteriological investigations carried on during the last few years have shed much light on the bacteriology of whooping-cough, an oval short bacillus resembling the influenza bacillus being generally regarded as the specific pathogenic factor. The biological details are still matters of contention, but control experiments (made by Reyher) are strongly suggestive of the specificity of Czaplewski's polarbacterium.

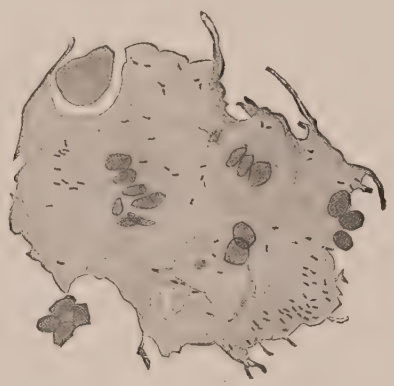
Concerning the *period of incubation* of whooping-cough hardly anything positive is known. According to the experience of most observers it varies between three and fifteen days. If three weeks after exposure to infection the disease does not develop, the child in question may be regarded as not infected.

With regard to the contagiousness of whooping-cough in the various stages of the process we find, especially among French investigators, divergent statements. Extensive observations and the importance of

greater prophylactic safety make it more advisable to regard whooping-cough as contagious during its whole course—that is, to keep a child suffering from whooping-cough isolated from healthy children so long as there is cough with expectoration. Recovery from whooping-cough almost always insures immunity for the remainder of life, according to an overwhelming array of observations. Analogous to those infectious diseases which have been etiologically more definitely investigated, this fact of immunity in whooping-cough may likewise be accounted for by reaction products evolved by specific bacterial metabolism. Against such purely theoretic considerations speaks the great uncertainty of our present etiologic investigation, in that children nourished from their mother's breast, even during their infancy, are not uncommonly affected, when we might expect a certain lessened susceptibility of the infant on account of the transference through the mother's milk of such antitoxin from the actively immune mother, who has had the disease.

It is possible that a child may become affected with pertussis a second time—an interval of complete health extending over years precluding a relapse of the first affection—but in such an event, the course of the disease is rapid and light.

FIG. 108.



Sputum in whooping-cough. Stained with 1 per cent. acetic acid and diluted carbol-glycerin.

Symptomatology.—For a description of the normal process of whooping-cough the hitherto usual distinction of the several stages may be retained with advantage, although a strict separation of the phases in a given case is frustrated by the frequent exacerbations and complications. We may retain the customary division into three stages, with a slightly characterized prelude of prodromal symptoms, such as lassitude, headache and disturbed sleep.

The first or catarrhal stage sets in with symptoms of an acute catarrhal affection of the respiratory organs, sneezing, conjunctival irritation, more or less severe cough, and sometimes with slight fever. Now and then a slight, enanthema-like injection of the palate and palatal arches is noticed. In this stage, as a rule, every auscultatory sign of bronchitis is wanting. In younger children, especially in such as incline to false croup, an attack of acute laryngitis may abruptly open the scene and in the next few days subside to the usual catarrhal symptoms. For one or two weeks, the temperature being normal and the general condition relatively good, the cough increases, becomes spasmodic, choking, more frequent by night than by day, and gradually

assumes the typical character of the whooping-cough paroxysms. Thus the catarrhal phase quite gradually glides into the convulsive stage. This first period of whooping-cough lasts one to two weeks, usually from seven to ten days.

While in the first phase of pertussis, especially during the first days, we find in the symptoms nothing characteristic of the disease and we are left in doubt as to the diagnosis; so that in the end only a positive history of exposure or the inefficiency of narcotics direct our suspicion to whooping-cough. The peculiarities of a single paroxysm and the objective results of an examination in the second or convulsive stage, will secure a positive diagnosis. The attacks occur either spontaneously or may be aroused by a variety of causes, such as emotion (anger, laughing, weeping), reflex acts (singultus, sneezing), swallowing of solid morsels, more copious meals, a draught of cold water, an air current, visual and auditory impressions (glaring light, shrill sounds), seeing or hearing of a whooping-cough paroxysm in another child. Spontaneously the paroxysms occur also during sleep, by night even more frequently than by day.

Older children, able to relate their sensations, describe aura-like prodromes introducing the paroxysm, as tickling or scratching in the throat, choking, eructation, suffocating distress, pressure behind the sternum, intense anxiety. These sensations impel the children to run to the mother, take hold of solid objects for a support, or rise rapidly from the bed. After a short pause in breathing and with some swallowing or choking movements a deep inspiration follows; and then begins without inspiration and rapidly repeated, a series of staccato-like, short and loud forcible expiratory efforts which through the auxiliary respiratory muscles, convulse the entire body. The face and the visible mucous membranes, meanwhile, become livid, the eyeballs protrude, a watery discharge oozes from the eyes, and the tongue becomes puffed up, deeply cyanotic, with scaphoid vaulting, and during the expiratory efforts projects from the mouth. Finally, after a succession of such short coughing efforts follows a deep, crowing inspiration, the rima glottis being narrowed, the intercostal spaces and clavicular fossæ contracted, and the hyoid bone drawn upwards. Immediately after there is a repetition of the spasmodic expiratory efforts, uninterrupted by inspiration continuing until again succeeded by a long-drawn, crowing inspiration. Finally, at the close of the attack with choking and vomiting, a scant, tenacious glairy mucus is expelled. Previously there may occur an apparent cessation of the paroxysm, a brief pause marked by a few quiet respirations, but very soon followed by a new attack of staccato efforts, by a repetition of the whole disease aspect,—a "reprise." (By many the whooping, crowing breathing is erroneously designated as reprise.) During the coughing fits, not infrequently involuntary

expulsion of feces and urine may occur, due to the vigorous force of the abdominal pressure.

The paroxysm, whose duration (usually 2 to 5 minutes) is apt to be overestimated by the awe-stricken, helpless layman, having terminated with the evacuation of tenacious mucus or without it, stronger and hardier children may be seen quietly resuming their interrupted play, their meal, or even speech, without any sign of distress. Others, on the contrary, after the attack exhibit lassitude, sweating, and acceleration of the pulse and respiration. Generally, if there are no complications, the subjective condition of the children is very good, far better than in the catarrhal stage, the cough-free periods affording them the quiet of full health. Subjective distress during the pauses, great exhaustion in spite of a small number of paroxysms, and especially elevations of temperature are always the first symptoms of incipient complications.

The number of attacks depends above all on the gravity of the affection and on constitutional factors, as well as on climatic and general hygienic conditions. In vigorous children and in uncomplicated cases the paroxysms may be only ten or even less in 24 hours, while on the other hand there are children who have to endure forty, or even fifty and sixty spasmodic attacks. The number of these paroxysms may be easily controlled and the attending nurse should be instructed to mark each attack by a sign on the history sheet.

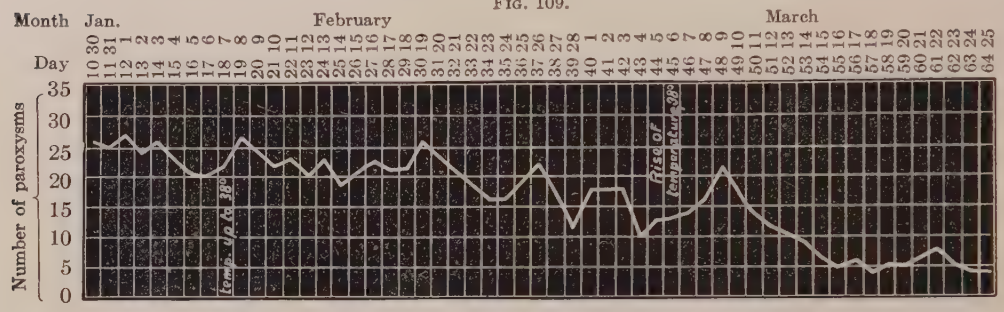
The convulsive stage in its course is characterized by three phases —an increase, an acme, and a decrease of the wave. The decrease manifests itself rather in a change in the severity of the single paroxysm than in a diminution of the number of attacks. The latter run their course entailing less effort on the part of the patient; the inspirations being more marked and effective, the spasmodic cough more rapidly draws to an end, and an earlier expulsion of the sputum with choking and vomiting occurs. Without sharp delimitation and gradually, the course of the disease begins to improve, reaching the stage of decline which is a second catarrhal phase.

The duration of the convulsive stage cannot be easily fixed, frequent exacerbations, even in uncomplicated cases, being apt to modify the course. Thus, we can determine the normal duration only in those cases which run a rapid course. Two to three weeks may generally be set down as the shortest duration of the second stage. But right here we have to emphasize that damage due to careless conduct, climatic conditions, severity of the infection, constitutional and especially complicating diseases may prolong the convulsive stage for weeks and months.

The last stage (stage of decline) marks the disappearance of the symptoms. The attacks occur more rarely, their course is milder and more rapid, a few coughing efforts constitute the whole paroxysm sug-

gestive of a severe productive bronchial catarrh, with mucus or mucopurulent expectoration. The daily number of paroxysms decreases, dropping to 3, 2, 1, until finally there occurs only one every few days. During this phase of whooping-cough the children feel quite well. But even in this period adverse conditions may cause a relapse into the

Fig. 109.



Whooping-cough of moderate severity. Marie W., seven years old.

paroxysmal stage and revive for days and weeks, all the symptoms of the convulsive attacks. In light cases this last phase of decline lasts from one to two weeks (Fig. 109).

In the pauses that are free from paroxysms, especially during the convulsive stage, we meet with symptoms of great diagnostic value.

Fig. 110.

Facies pertussea. Three-year-old girl. Third week of whooping-cough.

During a paroxysm there occurs a great congestion in the region of the superior vena cava and the tributary veins and lymphatics. This stasis, during a paroxysm, causes not only the cyanotic discoloration of the face and mucous membranes already described, but also a permanent distention of the lymphatic ducts and blood vessels, which may be seen in the pauses. Accordingly, the faces of children become bloated, particularly where there is loose subcutaneous cellular tissue; the upper and the lower eyelids stand out like pillows, and sometimes the eyeballs protrude slightly. In thin children the contrast between the scant fat of the body and the full, puffy face is often surprising. Hæmorrhages occurring during an attack, especially in the conjunctiva, are a consequence of the greatly increased pressure in the venous circulation. They may be so profuse that the sclera, so far as visible, appears blackish red.

Rarely, and only in cachectic children, does the skin of the face and body become blackened through extravasations of blood. In children with visible veins on the head and forehead, these vascular trunks become swollen as thick as a raven's quill.

Characteristic of whooping-cough is a sublingual ulcer or ulcer of the frænum. In children that have their lower incisors, we find a rhomboid or lancet-shaped ulcer of the frenum, with a thick white coating. This ulcer is formed during paroxysms by the protrusion of tongue, which at each coughing effort sweeps its under surface over the edges of the lower incisors. The sublingual ulcer occurs only in whooping-cough and at times becomes an important diagnostic aid. [This ulcer is seen also in other severe paroxysmal coughs in young children and is not diagnostic.—La F.]

A **physical examination** after a prolonged duration of the convulsive stage, reveals on percussion the signs of a certain pulmonary emphysema, the diaphragm standing deep, the intercostal spaces being fuller, and the upper clavicular fossæ vaulted forward. On auscultation, especially immediately before a paroxysm, we discover here and there a rhoncus, a fine rattling râle which disappears during the attack. As to the heart, provided an existing pulmonary emphysema does not affect the conditions on percussion, we notice an increase of the area of cardiac dulness towards the right, due to a dilatation of the right ventricle, frequently also an increased intensity of the second pulmonary sound, which is an expression of increased pressure in the lesser circulation. This congestion gives rise to intense venous hyperæmia in the whole respiratory tract and predisposes to hæmorrhages that are frequently observed. Owing to small vascular ruptures the expectorated mucus often appears flecked with blood.

According to Blumenthal-Hippius the condition of the urine is said to be diagnostically important even in the catarrhal stage. It is of a pale yellow color, strongly acid, of a high specific gravity (1.022 to 1.032) precipitating a large number of crystals of free uric acid. The daily quantity of uric acid secreted exceeds the normal by two or three fold. Co-existing febrile complications very much lessen the value of urinary findings as specific symptoms.

Glycosuria in whooping-cough has been frequently reported, but the excretion of sugar is far from being constant.

With regard to the condition of the *blood* in whooping-cough it may be said, according to recent examinations (F. Cima), that in simple pertussis leucocytosis occurs at the very inception, three times as many white blood corpuscles as in the normal condition being usually found. The intensity of leucocytosis runs parallel to the intensity of the disease. The increase in the number of leucocytes is greater in smaller children and during complications. With regard to the increase of the

several forms of leucocytes in the sense that the increase of the lymphocytes precedes that of the polymorphonuclear leucocytes, or that the number of the former decreases in proportion as the latter increase, no definite law has been observed. Consequently, nothing positive can be enunciated concerning the pathogenetic mechanism of the leucocytosis. In doubtful cases the blood findings may be of diagnostic value.

Examinations of the blood (by Crisafi) in whooping-cough are said to give positive iodine reaction in 80 per cent. of the cases. The iodophile granules are present in variable numbers, especially in the polynuclear leucocytes, less frequently in the eosinophiles and rarely in the lymphocytes.

Under certain circumstances we meet with *variations from the usual course* of pertussis. Here belongs the frequently shortened and scarcely characterized catarrhal stage in young infants. In such cases the spasmodic paroxysms set in rapidly, often in the first days of the illness. In children of the first year of life the characteristic stridulous inspiration following the succession of staccato-like coughing efforts is lacking, and the rarity or total absence of deep inspiration easily leads to apnœa and to syncopal accidents.

At the beginning of the convulsive stage, rarely during its whole course, the paroxysms at times set in with spasmodic sneezing, which presently passes into a convulsive cough, or, seldom, by itself constitutes the whole paroxysm, and terminates with choking and vomiting. Such a vicarious sneezing may persist during the whole of the whooping-cough.

A dyspeptic form, too, in which gastric and intestinal disturbances, along with spasmodic cough, are the salient features, has been observed by several (Jacobson), but such forms are dubious.

Sometimes the course of pertussis is characterized by such mild symptoms that only the existence of an epidemic and the history of exposure to the infection enable us to form a diagnosis. The paroxysms are but slightly marked, the cough resembles the vigorous and repeated expiratory efforts met with in bronchitis with scant secretion, and the whooping inspiration is lacking. In adults such forms (coqueluchette, forme fruste) are more frequent than in children. A correct recognition of such a case is not merely diagnostically important, but also for the reason that it might easily become the starting-point of a house epidemic and a further spreading of the disease.

In its symptoms pertussis at times becomes indefinite, when accompanied by febrile complications together with great prostration or considerable respiratory disturbances, and above all by bronchopneumonic infiltrations. In such conditions the coughing spells lose their characteristic peculiarities, and assume the form of short, dyspnœic

coughing efforts. Now and then the underlying affection betrays itself by severe cyanosis and jerky respiratory efforts ending in syncopal attacks.

The average **duration** of whooping-cough in light uncomplicated cases, varies between eight and twelve weeks. Still the majority of cases exceed this duration considerably. Exacerbations and various factors prolong each of the several stages. The season of the year at which the illness sets in, constitution, etc., may cause the whooping-cough to persist for months. Generally, during the warm, dry months conditions are more favorable. The observation has been made time and again, that weeks and months after the complete disappearance of the characteristic cough, a slight cold or a light bronchitis may revive in the child the typical cough of pertussis. This, justly as it seems, was explained by the assumption of a certain preparation of the nerve-paths involved in the cough reflex. The superior laryngeal nerve is regarded as one side of the reflex arc. An abortive, greatly shortened course of pertussis is said to occur at times, but it is very rare.

The **complications** of whooping-cough may be accounted for mainly by the mechanism of the paroxysms and the lesions that may be caused by it directly. These include subconjunctival hæmorrhages, epistaxis, vascular enlargement of the thyroid gland, ulcer of the frenum, and pulmonary emphysema due to increased expiratory pressure. Sometimes increased abdominal pressure leads to prolapse of the rectum and, in case the inguinal canal remains open, to inguinal hernia. Umbilical hernias, too, usually in small children, may occur during the process of whooping-cough. Rupture of the recti abdominalis muscle is a complication of rare occurrence.

Hæmorrhages of the mucous membranes of the nose, mouth and bronchi and multiple hæmorrhages of the skin may be regarded as effects, partly of the greatly increased intravenous pressure and partly of causes affecting and altering the vascular walls. But it is questionable whether increased pressure alone is able to produce hæmorrhages. Hæmorrhage also may occur from suppurating foci, from the sublingual ulcer, from moist eczema, from catarrhal areas in the nose, and from the ruptured drum membrane when the middle ear is involved. In subconjunctival hæmorrhages a preceding lesion of the vascular wall (conjunctivitis) can be assumed as a causative factor. In young children bleeding from the mouth is often due to biting of the tongue during a paroxysm.

On account of their frequency and importance in the prognosis of whooping-cough, complications of the *respiratory tract* deserve the greatest interest. They occur mostly in the convulsive stage. If in the intervals between the attacks the general condition of the patient is not good, if between the paroxysms there is dyspnœa, irritative cough, and

râles audible at a distance, we may infer that there is some complication of the respiratory organs. If there is also fever, then there is a capillary bronchitis or a pulmonary consolidation, as will be revealed by physical examination, which will show characteristic signs. As the lightest complication we find a diffuse catarrh. From this may develop, slowly or rapidly, a catarrh of the finer bronchi or a lobular infiltration of the lung.

Infancy especially predisposes to such complicating pulmonary affections, so that infants a few months old rarely escape. Children of any age affected with whooping-cough, who are weak with lessened resistance, or who are weakened by preceding or present constitutional diseases, have their chances of recovery vastly diminished by bronchopneumonia. Still the prognosis is never totally hopeless, not even for the youngest infants. The duration of bronchopneumonia is prolonged by the severity of the underlying disease and often by more or less frequent relapses.

During the course of whooping-cough, we meet quite frequently with symptoms that can be referred to *tuberculosis of the pulmonary and bronchial lymph-nodes*. These develop either primarily, betraying themselves by a certain debility of the organism; by emaciation; by a faded gray color of the skin; by febrile manifestations, and objectively by impaired pulmonary resonance in one or both intrascapular spaces (tuberculous infiltration of the bronchial lymph-nodes); or they pass on to a protracted and relapsing lobular pneumonia and thus become an early manifestation of latent tuberculosis. Tuberculous complications of the lungs are uncommonly frequent. These are almost never wanting in the post-mortem examinations of whooping-cough patients. Still they may reach a state of symptomatic quiescence and later on, after days and years, may terminate with an abrupt manifestation of miliary tuberculosis or tuberculous meningitis.

Chronic tuberculosis of the pulmonary or bronchial lymph-nodes is often encountered as a sequel when all the symptoms of pertussis have disappeared. A goodly number of tuberculous children date their affection back to whooping-cough.

Another typical complication of pertussis is *bronchiectasis*, a cylindrical dilatation of the bronchi, mostly multiple and accompanied by scar formation in the proximity. About the termination of bronchiectasis in childhood, not much is known. The significance of its progress is that it is rarely unaccompanied by the diseases of the lungs. Influenza may set in during the course of whooping-cough; bacteriological examinations by Jehle showing the presence of the influenza bacillus in twenty-four cases of pertussis always in the lungs and twelve times in blood. Mediastinal or subpleural emphysema, apt to spread in the subcutaneous tissue over the upper half of the body, is frequently

observed, disappearing after a shorter or longer time. In such cases the skin produces a sensation somewhat like an air cushion and crackles on palpation. Pleuritis of a serous or purulent nature occurs very rarely as a complication of pertussis.

Among the complications involving the *circulatory organs* the mildest ones are the previously mentioned congestive phenomena. As a result of congestion in the lesser circulation there may occur a primary dilatation with subsequent hypertrophy of the right ventricle. Only in greatly reduced children where the violent paroxysms of coughing are excessive is this hypertrophy wanting and, the heart not being equal to the demands in such cases, sudden heart failure may occur. Other complicating heart diseases, such as endocarditis and pericarditis, are very rare.

On the other hand, the peripheral vessels may at times sustain an injury from the toxin of whooping-cough. While no histological proof for such alteration of the vascular wall has as yet been forthcoming, certain clinical observations make it appear almost positive. Thus in the course of pertussis in weak children we notice a distinct œdema of the subcutaneous cellular tissue, although neither the heart nor the urine furnishes us any data for a satisfactory explanation. Moreover, we are inclined to assume that the factor of congestion alone is hardly sufficient for the production of cutaneous, subconjunctival, and intracranial hæmorrhages, but that the vascular walls must have a weakened power of resistance to be ruptured by increased blood pressure.

Among the *nervous complications* and sequelæ of whooping-cough, convulsions are the most frequent. Their typical course is characterized by the occurrence of clonic-tonic spasms during the convulsive stage and following a coughing paroxysm involving either a limited muscular area, or, as in epileptic attacks, all of the voluntary muscles, especially those of the extremities. Such eclamptic seizures usually follow the paroxysms, but at times they may occur between and independently of the coughing attacks. The convulsions are always multiple, a single attack hardly ever occurring. Frequently there coexists a fever. Between the several spasmodic seizures which are always attended with loss of consciousness there may persist psychical disturbances, stupor, and rigidity of the neck. The convulsions occur usually in children during the first year of life, who in other ways show a great irritability of the cortical centre. They indicate a severe and dangerous complication. During and between the eclamptic seizures, a remission of the whooping-cough attacks, both in number and intensity, is observed.

French medical writers mention, besides the convulsions (convulsions externes), also spasm of the glottis (convulsions internes) as a frequent complication of whooping-cough.

Clinically a typical picture of meningitis complicating pertussis is seldom met with. The rare occurrence of tuberculous meningitis is in striking disproportion to the frequency of tuberculous affections of the lungs.

Cerebral paralyses, either hemiplegic or diplegic, have recently become known as more frequent complications of whooping-cough (Hockenjos, Valentin, Neurath). They appear under the usual types of cerebral paralysis, either as monoplegias, hemiplegias, diplegias, sometimes combined with bulbar symptoms, or paralysis of the muscles of the eye or of the sense organs.

In the category of cerebral paralyses probably belong also disease pictures suggestive of multiple sclerosis following pertussis. Friedreich's ataxia likewise has been observed after whooping-cough. Among the psychic disturbances manifesting themselves during the course of pertussis we find insanity (in the form of hallucinations), complete imbecility (as shown by Baginsky's illustrative examples), symptoms of pavor nocturnus, etc. W. König saw permanent idiocy follow whooping-cough, but usually the psychic complications of pertussis are of a transitory character.

Sudden blindness after whooping-cough as a result of hæmorrhages into the anterior chamber or retinal detachment or central lesion,—the visual power usually soon returning,—auditory disturbances due to a complicating otitis media or to a direct lesion of the nervous apparatus, and disturbances of sensibility are among the sense disturbances that at times complicate whooping-cough.

Among the spinal cord disturbances may be mentioned a flaccid paralysis of distinct spinal character, which however cannot be readily explained (hæmorrhage, myelitis, poliomyelitis). Pains in the legs and loins, disturbances of sensation, difficulty in the evacuation of the bowels or urine may complicate the paralyses (Bernhardt, Luisada). Also polyneuritis (Faidherbe, Aldrich), Landry's ascending paralysis (Möbius, Hagedorn), and a case of so-called pseudotabes (Simionesco) have been observed after whooping-cough.

The anatomy of the *cerebral complications* of pertussis has recently been made the subject of close investigation (Neurath). Certain negative necropsy findings in well-marked clinical pictures, suggestive now of hæmorrhagic effusions or embolism, now of encephalitis, and again of meningitis, have given rise to the supposition that histological changes might be found which escape the free eye. It is undeniable that intracranial hæmorrhages are clinically more frequently diagnosed than anatomically verified. In such hæmorrhages a lesion of the vascular wall (called aneurysmatic dilatations by Vidal) plays a greater rôle in pathogenesis than the increased intravenous pressure.

Neurath found in a series of cases which during life presented symptoms mostly of cerebral irritation, a pronounced meningeal infil-

tration (mononuclear leucocytes), hyperæmia, and meningeal hæmorrhage from inflammation—findings analogous to those obtained in other acute infectious diseases such as typhoid fever, scarlet fever, and sepsis. He is inclined to attribute to this meningitis simplex a pathogenetic explanation of the development of a number of cerebral complications, in addition to the other anatomical data (embolism, hæmorrhage, encephalitis, etc.). This assumption seems to find a support in the results obtained by Bertolotti and others in lumbar punctures systematically performed on children suffering with whooping-cough. They found the puncture fluid to abound in mononuclear leucocytes.

With regard to the *digestive tract,* apart from a prolapse of the rectum mentioned previously, we find now and then gastric and intestinal catarrhs. Acute nephritis, sometimes ushered in with fever, is relatively seldom met with, but it may occur and be attended with uræmic symptoms. A complicating otitis media, occurring during the course of pertussis, probably starts from the nasopharyngeal space. Among the cutaneous affections we find, besides the hæmorrhages already mentioned, sometimes erythema, pemphigus, urticaria-like efflorescences (even non-medicamentous). They may exhibit a hæmorrhagic character.

Constitutional disturbances, anæmia and scrofula, are not rarely the sequelæ of whooping-cough. Their severity is in proportion to the severity and duration of the basal disease and the intercurrent affections.

Whooping-cough is often found associated with other acute infectious diseases. This fact can be accounted for only by an increased disposition, due either to the opening up of portals of infection or to a general weakening of the resisting powers. Especially in hospitals with insufficient accommodation for isolation, certain disease combinations are apt to occur. Foremost among the latter are measles, which more frequently follows than precedes pertussis. Varicella is likewise often a complication, whereas scarlet fever is rarely found associated with pertussis.

The **diagnosis** of whooping-cough in typical cases is easy, its symptoms and course as a rule being so characteristic that the history alone suffices. Still in many cases conditions have to be considered which may simulate whooping-cough.

The most important symptom of whooping-cough is the typical paroxysm. A spasmodic cough caused by tuberculosis of the bronchial glands may in numerous cases suggest a staccato cough. In such cases the course of the disease is important for a differential diagnosis. In whooping-cough the cough increases in a typical manner from the onset through the catarrhal stage (1 to 2 weeks) up to the beginning of the paroxysms, the latter usually terminating with vomiting. During the intervals the child feels well. The lungs, on examination, do not yield any results differing from the normal. On the other hand, in enlarge-

ment of the bronchial glands there is no climax, the coughing attacks preventing the recognition of the distinct whooping inspirations. Vomiting is rare, and the children convey the impression of being constitutionally stricken individuals (scrofulosis), and frequently exhibit hectic fever, while an examination of the thorax reveals dulness and bronchial breathing between the shoulder blades.

A pertussis-like hysterical imitation cough may be distinguished from true whooping-cough by the hysterical stigmata of the afflicted children, by the cessation of cough during sleep, by the absence of certain signs of pertussis (puffed face, sublingual ulcer). Whooping-cough may, without much difficulty, be distinguished from a reflex cough caused by hypertrophy of the tonsils, and from the symptoms provoked by inhalation of foreign bodies.

Finally, the history will exclude the existence of pertussis in those cases in which a catarrh, coming on long after whooping-cough has been cured, causes paroxysm-like attacks by bringing into activity the nervous paths which, through the ordeal of pertussis, have undergone a certain training.

The diagnosis of whooping-cough can be safely established by the physician when he has observed a typical paroxysm. We have certain methods of producing an attack. For instance, by introducing a spatula into the pharynx we may provoke choking and vomiting. But continued pressure with the finger on the trachea or thyroid cartilage usually suffices. Tickling the nasal mucous membrane or of the external auditory meatus accomplishes the same result.

Enumerating the positive data to be taken into consideration for a diagnosis of whooping-cough, we find:

1. After a slightly characteristic catarrhal stage the typical paroxysms set in with spasmodic expirations and few intervening crowing inspirations, terminating with the production of a tenacious, glairy mucus. Children in the first years of life commonly swallow their sputum. In whooping-cough the gagging and vomiting voids the sputum.

2. The cough is often more frequent by night. It may be caused by hearing and seeing a paroxysm in another child.

3. Results of an objective clinical examination are: lung signs negative in spite of the violent coughing; permanent lymphatic congestion (puffed face, swelling of the eyelids), sublingual ulcer, subconjunctival hæmorrhages.

4. Urinary symptoms (Blumenthal-Hippius), blood findings (leucocytosis).

5. Exposure to infection, existence of an epidemic, same disease in brothers or sisters.

6. Failure of antispasmodic medication (belladonna, morphine) in the customary doses, so long as the disease is on the ascent.

Diagnostic difficulties are encountered at the beginning of the catarrhal stage, as anything typical of whooping-cough is absent. In this phase an examination of the urine and of the blood and perhaps the history of exposure to infection may facilitate the diagnosis.

In very young children in whom the paroxysms pursue an atypical course, without crowing inspiration, and in the so-called "formes frustes" of pertussis, and finally when severe complications frustrate the paroxysms (pneumonia, convulsions), the history may at times enable us to make a diagnosis, yet it is frequently impossible to be positive at once.

Prognosis.—For vigorous older children whooping-cough is, on the whole, a harmless disease; but for the weak, chronically sick, and especially very young children, it is often of fatal significance. Because the younger ages are largely involved, the mortality from whooping-cough is statistically rather high. In the years 1895 to 1901, according to the statistical year-book of Vienna, 15,711 cases were reported as having occurred in that city, of which 1052, or 6.6 per cent., terminated fatally.

A comparison of whooping-cough with measles and scarlet fever for the three years 1899 to 1901 furnishes the following results:

Whooping-cough	6469 cases	444, or 6.86 per cent. died.
Measles	37,257 cases	1778, or 4.77 per cent. died.
Scarlet fever	7176 cases	631, or 8.79 per cent. died.

According to Presl the aggregate mortality from the following four infectious diseases for Austria during the year 1883 was:

Measles	0.45 per cent.
Scarlet fever	0.61 per cent.
Whooping-cough	1.09 per cent.
Diphtheria	1.41 per cent.

According to the above data whooping-cough occupies the second place among the more dangerous infectious diseases. The late sequelæ of pertussis (tuberculosis) evidently being left out of consideration, the mortality from whooping-cough probably is much higher.

As an illustration of the greater danger of exposure to infection during the earlier ages we present the following Vienna statistics for the years 1899 to 1901:

First year of life	1242 cases	322 or 25.3 per cent. died.
Second to fifth year	3139 cases	214 or 6.8 per cent. died.
Sixth to tenth year	1926 cases	75 or 3.9 per cent. died.
Eleventh to fifteenth year	135 cases	10 or 7.4 per cent. died.
Sixteenth to twentieth year	12 cases	0 .....0 .....died.
Twenty-first to twenty-fifth	2 cases	0 .....0 .....died.
Twenty-sixth year	13 cases	0 .....0 .....died.

Infants are generally the most endangered. Owing to frequent vomiting, their nutrition is easily affected. Moreover, they are exposed

to pulmonary complications, resulting in a mortality of 95 per cent. However, the very youngest of infants (in the first weeks of life) seem to endure the disease somewhat better—a fact observed by Porak and Durante during a domestic epidemic which had broken out in a pavilion intended for premature infants.

Of the greatest prognostic importance is the intensity of the affection, which may be influenced by various factors, such as reaction of the individual, character of the epidemic, season of the year, and hygienic conditions. An indication of the intensity of the disease is the number of attacks. According to Trousseau, over sixty attacks a day constitute a bad prognosis. Periods entirely free from attacks along with undisturbed well-being are the signs of a favorable normal course of the disease.

From the above-mentioned complications, besides pulmonary affections, a fatal termination may be induced by cardiac insufficiency, great losses of blood (epistaxis), and cerebral complications (hæmorrhage).

Every intercurrent infectious disease (measles, varicella, diphtheria) diminishes the prospects of a cure, both for the whooping-cough and the complications, even if a momentary diminution of the daily number of paroxysms simulates an amelioration.

The **prophylaxis** of whooping-cough in its main features is based on the details of its course and of the infection. The most important precautionary measures include the early segregation of the afflicted child from the healthy. As the symptoms of the initial stage are usually ambiguous and not characteristic and as they must certainly be regarded as infectious, the pressure of an epidemic of pertussis should warn us to look upon every coughing child as a whooping-cough suspect.

The prophylactic measures belong partly to the domain of public hygiene, and partly to the individual or family. Above all, every child suspected of whooping-cough should be kept away from the school, nursery, or kindergarten, and its brothers and sisters, as well as the other inmates of the house, should be segregated during the entire duration of the disease, unless they have had whooping-cough themselves and are removed from all contact with the patient. Moreover, superintendents of public playgrounds and parks should exclude children sick with whooping-cough, or reserve grounds for them provided with cuspidors containing disinfectants. Separate compartments in railroad cars, as recommended by many, would be a desirable arrangement, whereas the use of public vehicles should be prohibited.

Private prophylaxis includes strict isolation of the affected child from the healthy ones in order to prevent the spread of the disease. It might not be unwise in certain cases, provided the age is sufficient and constitution good, to allow the brothers and sisters to be visited by the

infection, in order to guard against the possibility of a future invasion of the house after months or years. Indirect transmission, through soiled objects, must likewise receive proper attention.

Prophylaxis also includes protection from a whooping-cough epidemic in case of change of location of the stricken individuals. Thus during the hot season many summer resorts and sanatoria that are largely frequented are apt to be endangered, so that the exclusion of a newly arrived child stricken with whooping-cough is a justifiable measure of self-protection.

When received at a hospital for contagious diseases, every child suspected of whooping-cough must be kept away from the wards intended for other diseases, and thus by adequate isolation a domestic epidemic be guarded against, as it is well known how fatal any combination with other infectious diseases may become. Considering the high whooping-cough mortality in hospitals, the admission of children stricken with pertussis should wisely be confined to such cases as come from the very lowest of social and hygienic surroundings and for such individuals hospital treatment would indeed signify a relative amelioration.

When the whooping-cough has run its course, all the rooms should be thoroughly disinfected.

Treatment.—The therapy of pertussis rests nowadays on mere empiricism. An etiological treatment was attempted by Manicatide (whooping-cough serum), but the theoretical basis of his curative serum s still very questionable and practical results of a convincing nature are wanting. Drug treatment has at its disposal an arsenal of means that increases from one day to another. Theoretical considerations, advertisements, a personal liking for a certain remedy, etc., are frequently the determining factors that bring the highsounding recommendation accompanying the latest drug. For the valuation of the efficacy of a medicament proper attention must be paid to the stage of the disease at which the remedy is tried and to the external factors influencing the disease, such as hygiene, climate, etc.

Of especial value for the treatment of whooping-cough are *hygienic measures*. In a fresh, warm, dust-free atmosphere without drafts, a numerical decrease of paroxysms may always be observed. A rational fresh-air treatment without moving about much and where all chance of chilling is carefully avoided usually brings about an improvement; nay, often the paroxysms disappear so rapidly that an abortive course suggests itself. The much-vaunted change of air is of value only if it is equivalent to an improvement of the climatic conditions. During the inclement season or when complications and febrile temperatures preclude out-door life, the so-called two-room system is recommended, one room being thoroughly aired while the sick child stays in the other.

By a proper ventilation of the bedroom at night any increase in the number of paroxysmal attacks during the night can always be avoided. The temperature of the room must not be allowed to fall below 52° F. nor to exceed 60°F. The child is to be kept in bed if the course of the disease is very severe and debilitating, and particularly if there are febrile complications. During the cool season it is often advisable to warm the night clothes and the bed during the night.

The clothing of the child afflicted with whooping-cough should correspond to the season of the year and not depart therefrom in any direction. The fastening of the clothes must be such that suspenders, braces, strings, bands, or straps do not interfere with the respiratory function and the mechanism of coughing.

It is important to counteract any failure of the nutritive condition by a judicious regulation of the meals, both with regard to their frequency and quantity and quality. All crusted, hard, too strongly tasting or smelling food (which gives rise to paroxysms) must be avoided. Too copious meals easily incite coughing. Frequent small meals are therefore advisable. Many children can readily retain, without fits of coughing, food of the consistency of gruel or pap, while others do better with more liquid food. This factor must not be left out of consideration. The best time for administering food is after a paroxysm. Medication recommended for the whooping-cough should display either an expectorant influence or an antizymotic or antispasmodic action. With regard to the mode of application, it may consist of inhalations, insufflations, pencilling of the pharynx, nose, or larynx, embrocations, internal remedies, and in physical curative methods.

For inhalation carbolic acid is much used, in a ½ to 2 per cent. solution, by means of an inhaling apparatus or by suspending cloths dipped into a 10 per cent. solution; aqua picea, oleum terebinthinæ, lignosulphite, salicylic acid (½ to 2 per cent.), thymol (0.02 per cent.), benzol, (0.01 per cent.), naphthalin, chloroform (2 to 4 drops in a cup of warm water), formalin (hygeia lamp), cypress oil (according to Soltmann 10 to 15 drops of a 20 per cent. alcoholic solution to be dripped on bed clothes and underwear), etc.

Insufflations of boric acid, benzoin, sodium sozo-iodolate, orthoform, quinine (1 : magn. ust. 10), are on account of their cough-inciting properties a two-edged medicament; likewise pencilling with solutions of quinine (10 per cent.), resorcin (2 to 3 per cent.), cocaine (10 to 20 per cent.), and sublimate (one per cent.) which may be used for older children. Among the external methods of treatment are included inunction with antitussin (difluor de phenyl, a piece of the size of a pea over the skin of the back) and the administration of enemata (quinine).

More frequent and usually more successful is the use of the internal remedies, as an auxiliary of which sometimes one or the other of the

above methods is employed. The transitory success of the medicaments recommended is often observed and makes a repeated change of the prescription advisable, but none of these insures any safe and lasting benefit.

In the catarrhal stage mild expectorants bring relief—liquor ammon. anisat., senega, ipecacuanha, etc.; when the cough is more intense, such antispasmodics as are customary for childhood (as althæa, belladonna, and very small doses of codeine or morphine). In the paroxysmal stage we may select one or the other of the antizymotics and narcotics.

A favorite remedy, in use for a long time, is quinine and its derivates: quinine [sulphate of quinine 0.05 to 0.07 Gm. (1 gr.) for children below one year; 0.07 to 0.15 Gm. (1–2 gr.) for the second and third years; 0.15 to 0.25 Gm. (2–3½ gr.) for the fourth year and above, one powder three times daily]; euquinine [tasteless, 0.1 to 0.5 Gm. (1½–7½ gr.) three times daily]; aristochin [three times daily as many decigrams as the child is years, maximum daily dose 1.2 Gm. (18 gr.)]. The quinine preparations are best given in full doses for three days, after which in half doses for six days, and then discontinued for a few days. They may also be administered in suppositories, to spare the stomach.

Among remedies having an action similar to that of quinine, but a more distinct one on the nervous system and the heart, and favorably influencing the number of paroxysms, may be mentioned: antipyrin, tussol [amygdalate of antipyrin, 0.05 to 0.5 Gm. (1–7½ gr.) three times daily], citrophen, salipyrin, antispasmin (1.0 : aqu. amygdal. dulc. 10.0, three to four times daily 5 to 20 drops), pertussin (3 to 4 teaspoonfuls a day) coclussin (10 to 25 drops several times a day). The antispasmodics are frequently used as whooping-cough remedies, among which belladonna and its derivates are the most prominent.

Belladonna often effects a surprising reduction in the curve of attacks, but fails after prolonged use. At the first sign of any symptoms of intoxication it is advisable to discontinue the preparation (vertigo, tickling in the throat, dilatation of the pupils). Belladonna may be used by itself [pul. radic. belladonnæ 0.1 Gm. (1½ gr.) or with sulphate of quinine, 0.5 Gm. (7½ gr.) sacch. 2.0 Gm. (30 gr.), divided into ten powders, one powder two to three times daily; or its infusion, 0.5–1.0 to 180.0 (7½–15 gr. to 6 oz.), a small spoonful every two to three hours; extract of belladonna, 0.02–0.1 to 10.0 c.c. (⅓–1½ gr. to 2½ dr.) of aqu. amygdal. dulc., 10 drops every three hours, or extract belladonnæ 0.1 Gm. (1½ gr.), sacchari 2.0 Gm. (½ dr.), divided into ten powders, 3 to 4 powders daily; also atropine, 0.005 to 100.0 c.c. ($\frac{1}{12}$ gr. to 3½ oz.) of water, twice daily 1 teaspoonful. A sedative action on the whooping-cough is exercised by the bromides, 1–3 Gm. (15–45 gr.) a day; bromoform, for infants 3 to 4 drops, for older children 5 to 7 drops, three to four times

daily; fluoroform, a 2 to 2½ per cent. aqueous solution; a coffee—small —or teaspoonful according to the age three to four times a day. Thymobromal (a maceration of thyme herb, folia castaneæ vescæ, radices senegal, to which bromoform is added, 15 to 20 drops daily).

If the cause of the disease is severe and all the attempted remedies prove inefficient, we have to resort to morphine and the allied alkalies, especially when it is necessary to procure rest for the child after several sleepless nights with many paroxysms. This object may be accomplished by cautious doses of morphine itself, 0.0025–0.005 Gm. ($\frac{1}{30}$–$\frac{1}{12}$ gr.) a day; or by codeine, 0.005 to 0.01 Gm. ($\frac{1}{12}$ to $\frac{1}{6}$ gr.); or by heroin, 0.0025 to 0.005 ($\frac{1}{30}$–$\frac{1}{12}$ gr.) twice a day. A codeine preparation (3 per cent. codeine and 97 per cent. extract of elecampane root) has recently been warmly recommended.

The saccharated extract of thymus, 2 to 3 spoonfuls a day; hydrochloric phenocollum [0.5–3.0 Gm. (7½–48 gr.) to 90 per cent. of a decoction of althæa and 10.0 of cherry syrup, 1 dessertspoonful every two hours] and a great many other remedies are said to have a specific influence on whooping-cough.

Many observers claim to have seen successful results from certain physical curative methods, and a trial of such under certain circumstances can certainly be recommended. In this category belongs respiration in compressed air (in the pneumatic cabinet). Regular administration of tepid baths and carbonic acid baths, will not fail to influence favorably the general condition, if not the pertussis itself.

Within the last few years vaccination has been warmly recommended by many as a prophylactic and therapeutic agency against pertussis. It is claimed to bring about a favorable change in the course of whooping cough and at times to diminish the susceptibility to infection. But control experiments have proved vaccination to be inefficient.

Intubation (according to O'Dwyer) is rather too energetic a method to find many advocates. Yet it may be beneficial when the course of the whooping-cough is severe.

The treatment of the complications of whooping-cough depends upon the nature of the complicating disease. A prophylactic measure may be noted which is said to be able to prevent the development of capillary bronchitis, namely, Schultze's swinging as recommended by Raudnitz.

ACUTE ARTICULAR RHEUMATISM

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By acute articular rheumatism, we understand a febrile disease of the joints characterized especially by transitory attacks of inflammation which pass intermittent from joint to joint and practically never result in suppuration. To these are added as further characteristics the frequent involvement of the serous membranes, especially of the endo- and pericardium, as well as the specific influence of salicylate preparations on these joint ailments.

Various forms of polyarthritis were formerly included in the description of acute articular rheumatism. These diseases, now designated as rheumatoid (Gerhardt) are known to be sequelæ of a variety of infectious diseases, the specific irritants or toxins of which have produced them. Although they are probably closely related to rheumatic joint diseases, they will be treated in a special article, because thorough scientific and therapeutic knowledge covering them is of special interest.

Particularly characteristic of acute articular rheumatism in childhood, is the milder and shorter course of the joint manifestations, while involvement of the heart and lasting injury to it is more frequent than in adults. Furthermore, we notice especially in children predilection for certain areas, for example the joints of the cervical vertebræ; as well as such complications as the formation of subcutaneous nodules and chorea minor.

Etiology.—Acute articular rheumatism is a disease found all over the world. Its appearance is commonly uninfluenced by such factors as natural phenomena, character of the soil, and underground water. Nevertheless, frequent observations have shown that single epidemics or a succession of epidemics occur from time to time, although contagion by transmission has hardly in any case been proven. It is a remarkable fact that brothers and sisters can be attacked almost simultaneously, and judging from a series of observations extending over a number of years, the disease has been found quite frequently to seek its abode in certain houses. In a very few cases, and even these admit of doubt, transmission from the affected mother in childbirth has been reported.

If we are inclined to give some credence to the statement that acute articular rheumatism is an infectious disease, probability becomes a certainty when we closely observe the clinical phenomena, the fever, the complications relative to the endo- and pericardium, the pleura and the skin.

A specific causative factor has, as yet, not been found. For the present it must remain undecided whether in rheumatic polyarthritis we have to deal with a case of attenuated sepsis which might be caused by various germs (strepto-, staphylo-, or diplococci) or whether it is a case arising from an inherent exciting cause.

Moreover, there is another question to be determined, whether the manifestations in the joints (and of the serous cavities) are the result of the causative agent itself, or of its toxin.

Menzer asserts that the oral cavity is the portal of entry (as do also Singer and Meyer) and considers the inflammation in the joints and serous cavities as reactive reparative efforts of the organs attacked by the causative agents (streptococci).

Although the real etiological factor of the disease is yet unknown, we do know a number of *predisposing causes*, which are co-operative in the development of the disease. In the first place "catching cold" must be mentioned, the influence of which, not only in a first attack, but also in cases of relapse, can not be doubted. Very often the onset of the disease follows a single severe exposure or wetting, particularly of the feet. Cold damp dwellings play an important part in the development of infection. A constant influence of the seasons upon the number of cases has not yet been proven. No doubt hereditary influences may here play an important part. They are absent in some cases. It is by no means rare that in certain families rheumatic diseases run through several generations with an increasing ratio. That a traumatism of the joints can directly change to true articular rheumatism, has often been observed, especially in children (Biedert, Marfan, Boseck). The sex of the children seems to be without noticeable influence.

As to age, it may be said that the latter half of childhood is by far more frequently attacked by the disease than the earlier; in fact its appearance is even rare before the fifth year. We have however seen it come as early as the second or third year of life, and even in the nursing period some well substantiated cases have been recorded. Even if the disease has been cured, it increases the predisposition to subsequent attacks.

SYMPTOMS OF ACUTE ARTICULAR RHEUMATISM

Prodromal Symptoms.—Very frequently manifestations of an indefinite nature precede the outbreak of the disease itself, as languor, anorexia, dragging pains in the joints, and sometimes even abdominal

pains. Catarrhal or follicular angina appear as forerunners in a number of cases; but as far as clinical observations go they do not play such an important part as some recent authors ascribe to them. Often all prodromal symptoms are wanting, and the disease appears with or without vomiting in its full severity.

Joint Localization.—The knee- or ankle-joints are those which are primarily and most frequently attacked. Often, however, it is the elbows, wrists or shoulders, which initiate the disease. But sometimes the hip or the cervical vertebræ, and less frequently the joints of the small fingers or toes, are first attacked. As in the case of adults, the disease passes in its course from joint to joint, either symmetrically or often advancing irregularly in its progress. More than one joint is always attacked. When new joints are involved, the inflammation in those primarily affected as a rule recedes, but it may persist. It is not rare that a joint may, in the course of the disease, be repeatedly attacked. The attacks in an individual joint will generally last only several hours; a duration of two or three days in childhood is the exception. In the disease which is characterized pathologically and anatomically as a serous synovitis, the joints involved are particularly painful upon active and passive motion, and tender to palpation. Still the pains are seldom so intense as to cause complete immobility of the joints. An exception to this rule is that in children the frequent localization in the hip-joints may cause an intense degree of suffering. The *objective symptoms* of inflammation in children are apt to be moderate, slight swelling and periarticular œdema are often found, while intense redness and copious effusions are absent as a rule. Pain is often the only symptom.

The temperature does not follow any definite type, still it seems that invasion of new joints or the serous membranes is accompanied, as a rule, by a higher degree of fever; also mild cases often begin with a single rise of temperature, over 39° C. (102° F.); in severer cases the fever may last several weeks, but this is the exception. In general, however, particularly under the constant influence of salicylate therapy, the temperature returns after a few days to the normal, although the rectal temperature in the evening may continue for some time at 37.6°–37.9° C. (99.6°–100.2° F.).

The *general condition* of the patient in the beginning is often considerably affected. Children show an unusually distressed countenance; the tongue is coated and pasty, the skin becomes remarkably pale, such palor is often seen from the outset of the disease, but especially if the pain continues for any length of time. Careful examination of the blood does not show any special findings aside from an insignificant occasional leucocytosis (Baginsky). The marked tendency to profuse acid perspiration common in adults, is frequently observed in children, although in a lesser degree. The bowels are generally constipated; there is

severe, tormenting thirst, with anorexia and insomnia. The general condition depends upon the course of the fever; in most cases it improves by the end of the first week.

The *duration of the disease*, as regards the joints, seldom exceeds ten to fourteen days; often the whole illness is over in five to seven days. As a special peculiarity of rheumatism in children it must again be pointed out that the joint disease with its entire symptom-complex may take an uncommonly light, almost afebrile course without seriously influencing the general behavior of the patient. Nevertheless, these abortive cases may be attended with very severe heart complications.

Complications.—As complications of acute articular rheumatism we here classify a series of processes which either positively or with more or less probability may be taken to be nothing more than further manifestations of the disease developing from its irritant poisons. First in importance must be mentioned the *involvement of the heart*. The frequency of cardiac complications characterizes rheumatism in children as a serious dangerous disease. More than half of all cases leave behind them permanent cardiac defects. The heart remains normally active during the entire course of the disease only in a small minority of the patients. This explains the disproportionately high pulse rate which we see in nearly all cases, even if clinically there can be demonstrated no defect in the heart itself. In most cases (from 60 to 80 per cent.) verrucose endocarditis results, localized in the great majority of cases at the mitral valve. Only by careful and exact clinical observation can we determine the occurrence of such an unfortunate development. Then there appear recognizable heart murmurs, which are generally accompanied by rise of temperature, irregularities or other changes in the action of the pulse. Since children under eight years of age seldom suffer from intense localized pain and palpitation, it may happen that children whose acute rheumatism has had an abortive course are first brought for medical treatment with signs of beginning cardiac insufficiency.

Endocarditis.—Endocarditis usually appears at about the end of the first week, and often even sooner. But in childhood there are also cases in which the endocarditis precedes the localization in the joints. Indeed endocarditis alone may be discovered, and only later when attacks of articular rheumatism follow, does the thought suggest itself, that the heart disease may be of a rheumatic nature. In the very early period of childhood, such a course is apt to occur quite frequently (Schlossmann). The possibility that abortive articular rheumatism has existed must therefore always be borne in mind.

Pericarditis.—Next to endocarditis, pericarditis is an important and most fatal complication. The involvement of the pericardium too, is more frequent in children than in adults; it manifests itself in about

10 to 20 per cent. of all cases, being nearly always associated with endocarditis. It is by far the most frequent cause of death in children having rheumatism.

With serous or even serofibrinous pericarditis, a case of cor villosum may develop, or a partial or complete obliteration of the pericardium with injurious effect upon the heart action may follow. And it is just this combination of valvular defects and pericardial adhesions, together with a myocarditis which is quite natural in such cases, that may bring about a fatal termination to the disease, often so insidiously begun, after weeks, months or years of suffering.

Other Complications.—Pleuritis of a serous or serofibrinous nature is a complication which is not rare in chidlhood. Of course this occurs only in severe cases, and then only in combination with pericarditis. It is apt to be non-malignant, and even a considerable exudate may be readily absorbed. Other still rarer complications in childhood are bronchitis, pneumonia, and nephritis.

Angina and nose-bleeds in the course of articular rheumatism are often met with in children. Occasionally a purpuric rash appears in the neighborhood of the affected joints.

A peculiar relation hitherto unexplained, exists between chorea minor and the articular rheumatism of childhood. It may precede the joint disease, but in the majority of cases it follows it. Like articular rheumatism, it is often complicated by verrucose endocarditis, and like the latter, chorea seems, in some cases, to take the place of joint attacks. A more complete description of the phenomena may be found in the section on chorea minor.

As to the relation of erythema exudativum multiforme and erythema nodosum to articular rheumatism I must refer to the respective sections in this book. Certain eye affections, more or less correctly classified as rheumatic, *e.g.*, iritis, skleritis, cannot be discussed here.

SPECIAL COURSES OF THE DISEASE

Some conditions peculiar to childhood may be mentioned here. Severe psychical and nervous derangements, as hemi- and paraplegia and the so-called *hyperpyretic form*, which usually with a temperature of 41°–43° C. (105.4°–109° F.) leads to death, have been observed in childhood, but only in very rare cases.

The localization of the disease in the joints of the *cervical vertebræ* often appearing with a rheumatic torticollis, is not rare in childhood; it is often misinterpreted as a purely muscular affection, as has been emphasized by Lannelongue and Marfan. Sometimes it may be the only seat of the disease, resisting all therapeutic measures with a pertinacity unusual in childhood and may in this way lay the foundation for a subsequent chronic arthritis.

A form of rheumatism almost peculiar to childhood is *nodular rheumatism*, which was first described by Meynet in 1875 and obtained greater publicity through the writings of Rehn and Hirschsprung. Over 40 cases have been reported, mostly by English authors. It usually occurs in the course of an attack of acute articular rheumatism, or sometimes during a relapse, generally in the third week or later from the onset of the joint symptoms. Subcutaneous nodules appear under the unchanged skin, developing very rapidly, often over night. They are more or less symmetrically located in the vicinity of the joints and along the tendons but may be in distant parts of the body, *e.g.*, on the bones of the skull. They are the size of a pin-head, or even a nut, and only rarely are firmly attached to the periosteum or tendons. They are rather sensitive to pressure and consist of fibrous, or partly fibro-cartilaginous tissue (Henoch, Hirschsprung, Barlow). Drewitt considers them analogous to the nodules of rheumatic endocarditis. Their number varies from one to more than fifty. The nodules generally soon disappear. Rarely their re-absorption extends over weeks or months in the severer cases of rheumatism, which are almost always complicated with endo- or pericarditis. Some cases with chorea were repeatedly observed and one case had also erythema multiforme.

Course and Prognosis.—Most cases of polyarthritis in children get well quickly and completely; on the other hand, it may be with a defect of the cardiac valves. Relapses are frequent in children, and it is not uncommon to have endocarditis develop during a second or third attack, if a previously existing lesion should grow worse. Death occurs almost without exception from severe cardiac complications; particularly pericarditis, but occasionally from multiple emboli. In rare cases swelling and stiffness may remain in some of the joints. Repeated relapses may cause a transition into the chronic articular variety.

So far as life is concerned, the prognosis is more favorable in children than in adults. It is, however, entirely dependent upon the severity of the heart complications.

Diagnosis.—The diagnosis of acute articular rheumatism is usually readily made. Nevertheless there are cases in which difficulties occur, and where a false diagnosis might be fatal. This applies especially to those forms of rheumatic arthritis in which prompt surgical interference is indicated, as in the cases of septic and pneumococcic arthritis. At any rate the possibility of the presence of a rheumatoid condition must be considered, and of course one must exclude scarlet fever and gonorrhœa.

The characteristic symptoms of pneumococcic arthritis will be described below. The diagnosis of rheumatic arthritis is based in general on the migratory attacks in the joints, the character of the inflammatory process, the polyarticular localization and the beneficial

influence of salicylate therapy. Endocarditis, if present, it is true, does furnish in the case of rheumatoid conditions, a most valuable and an indisputable element. Cases of hereditary syphilitic joint affections deserve special attention. They follow a subacute course and, attacking the two knee-joints symmetrically, are often incorrectly diagnosticated. Further details regarding these cases will be given on page 500. In a case of syphilitic osteochondritis, only a careless examination can possibly lead to a wrong diagnosis.

From a differential standpoint it may be said that an atypical attack of articular rheumatism, beginning with severe pain in the hips, may at first impress one as a severe case of suppurative coxitis. In one case under my observation the diagnosis of sciatica was also erroneously made. Sometimes the distinction between spinal caries or beginning retropharyngeal abscess and rheumatism of the cervical portion of the vertebral column may create difficulties. The presence of osteomyelitis, too, may occasionally appear probable. An accurate local examination as well as the course of the disease will readily clear up the diagnosis.

In little children and infants who, by the way, are more frequently subjected to all kinds of rheumatoids than to true acute articular rheumatism, infantile scurvy must occasionally be differentiated from polyarthritis. Careful examination of the gums and urine and localization of the pain in the limbs will prevent a wrong diagnosis. Articular swelling, which sometimes occurs after the injections of a curative serum, is directly traced to its cause by a knowledge of the history. It must again be stated that an abortive course of articular rheumatism is often called growing pains, and only later on, because of an endocarditis or chorea developing, is it correctly diagnosticated.

Prophylaxis is especially important in children who either have already had an attack of articular rheumatism or chorea, or who are descendants of rheumatic families. Dry and healthy habitations and avoidance of exposure to cold or wetting are very essential factors. Often the wearing of woolen or merino undergarments is to be recommended. A hardening process by means of hydrotherapy carefully begun under systematic medical guidance is particularly beneficial.

Treatment.—Two conditions must always be complied with : rest in bed until all manifestations cease and a constant regulation of the temperature of the room at 14°–15° R. (62°–65° F.). Every opportunity to acquire a cold subjects the patient to the possibility of a relapse and a prolongation of his sufferings. During nursing, and the changing of linen, etc. this possibility must be carefully watched, as the profuse perspirations which are present in the disease, or possibly also the salicylate treatment, may enhance the danger of chills and colds. The bed should stand in the most protected part of the room and above

all not close to a cold wall. Woolen garments, even when in bed, are often of advantage. Warm but not too heavy bed covering is important, and should be the special care of the nurse, particularly with the younger children, who are apt to uncover themselves.

Diet.—At the height of the fever: bouillon, milk, wheat bread, barley or oatmeal broth, or pap; at the same time plenty of fluid in the form of lemonade and soda water. When the temperature falls, vegetables, meat and eggs are permitted.

Salicylic acid is specifically effective for controlling the fever and the articular phenomena, and is best administered as salicylate of soda or aspirin.

Effective action against the invasion or severity of the heart complications is unfortunately not assured either by the above or by any other measure. At the outset not too minute doses should be given, to smaller children 0.25 Gm. (about 5 gr.), to larger children 0.5–0.8 Gm. (7½–12 gr.) three to four times daily, as a powder or in aqueous solution. When, after the lapse of 1 to 2 days, the symptoms have vanished, the daily dose of 1 Gm. (15 gr.) for older children, and 0.5 Gm. (7½ gr.) for younger ones may be persisted in for 6–8 days more, in order to avert another attack in the joints.

℞ Aspirin ..... 0.5 ..... gr. vii
D. t. d. vi.
Sig.—Three times daily—½–1 powder.

℞ Salic. sod ..... 5.0–10.0 ... ℥iss–iiss
Tinct. aurantii cort. ..... 2.0 ..... ℥ss
Aq. ..... 100.0 ..... ℥iii
M. D. S.—One half to one teaspoonful three times a day.

This medication is followed by more or less profuse perspiration. Other secondary effects hardly occur if the above-mentioned doses are adhered to, excepting ringing in the ears, which, however, is not an indication to discontinue the salicylate preparations.

Heubner observed nose bleeding in a few cases, and we have seen albuminuria appear twice, which slowly vanished after discontinuing the salicylates. In case salicylic acid or aspirin prove ineffective, one of their substitutes may be successful, as phenacetin, antipyrin, salol, salipyrin and lactophenin, in such doses as are appropriate for children. In these cases, which however, are rare, even the above-mentioned remedies may fail, and it is then always well to reconsider the diagnosis. We may often be forced to conclude that we have a case of rheumatoid before us, or else one of those sad cases with a tendency to change into the severe chronic form, the treatment of which will be described on page 506.

In connection with the internal, a *local* treatment may be required if the pains are severe. Simply enveloping with cotton wadding or

immobilizing in splints is often found to give great relief. By means of "mesotan" local salicylic treatment can be had in place of the internal salicylic doses.

℞ Mesotan ..... 20.0 ..... ℥v
Ol. Ricini ..... 30.0 ..... ℥i
M. D. S.—3–5 Gm. (½ to one teaspoonful) painted over the joints. (One must be on the lookout, however, for dermatitis.)

If after the acute stage has passed, swelling or stiffness of individual joints remains, inunctions with ichthyol-vaseline (10 per cent.) or Priessnitz compresses followed by massage may render good service. If there is the least suspicion of ensuing endocarditis, the measure most indicated and most important, though very difficult to carry out with children, is absolute bodily rest; with the customary application of icebags, it is important to avoid needless uncovering of the patient, or accidental wetting, lest a relapse of the joint symptoms be caused. With regard to an established endocarditis, pericarditis, etc., we refer to their relative sections.

Rheumatismus nodosus requires no special method of treatment. For a rheumatic involvement of the cervical portion of the vertebral column, it is advisable, if salicylic therapy does not bring speedy recovery, to resort to the applications of warm poultices and carefully conducted massage. For severe cases, some new methods of treatment which have been recently proposed may be briefly mentioned here: The intravenous (Mendel) or intra-articular (Bouchard) applications of salicylic acid; scarification and cauterization of the tonsils (Gürich); the use of streptococcic serum (Meyer, Menzer). Menzer expects, through his serum, to be able to reduce the frequency of cardiac involvement. The value of these methods is up to the present time, as far as adults are concerned, open to discussion; their general application in the case of children would be therefore much less advisable.

SPECIFIC ARTHRITIDES

RHEUMATOIDS—PSEUDORHEUMATISM

Multiple joint infections occur in the course of, or as a sequel to, many acute infectious diseases. In some cases the specific microorganism can be found in the secretions of the joint. A consideration of the several characteristic forms is of importance from a diagnostic and therapeutic standpoint. These infections are not uncommon in childhood and infancy. Among them may be mentioned typhoid, diphtheria, cerebrospinal meningitis, German measles, influenza, etc. The most frequent and distinctive forms are described below.

SEPTIC POLYARTHRITIS

I wish to refer here only briefly to suppurative inflammatory joints, associated with general sepsis. They are to be found in all periods of childhood, especially in nurslings, where a puerperal or umbilical infec-

tion may be its basis. We may also call attention to (secondary) streptococcic sepsis following scarlet fever, which frequently produces purulent arthritis. The joint symptoms in themselves do not manifest the presence of sepsis. In doubtful cases the high leucocytosis will preclude rheumatic polyarthritis. Diagnosis by exploratory puncture and a microscopic examination of the pus should be made immediately, since a prompt incision may effect a cure, even in nurslings (comp. Schlossmann).

GONORRHŒAL ARTHRITIS

In comparison to gonorrhœal vulvitis which, according to our experience, is rather frequent, gonorrhœal joint inflammation in children is decidedly rare. It appears more frequently as a sequel to purulent ophthalmia; and to gonorrhœal urethritis in boys. Arthritis appears most generally in the second or third week subsequent to the local attack. It is especially apt to attack the knee-joints. Among others the temporomaxillary and sternal joints may likewise be attacked. The articulations are usually very painful, highly reddened and swollen. Puncture shows seropurulent fluid, in which the presence of gonococci of typical stratification can be found under the microscope or even by culture. High irregular fever usually accompanies the affection. The course of the disease is with children and infants in particular usually a rapid one, seldom exceeding two or three weeks, and recovery, even functional, is as a rule complete. Complications with tendovaginitis (Seiffert) endocarditis (Chiaso and Isnardi, Schlossmann, Hermann) and pleuritis (Mazza, Bordoni-Uffreduzzi, Chiaso and Isnardi) occur, but even these affections appear in children as non-malignant and curative. A combination of skin-metastases in the form of vesicles and papules is described by Paulsen, with this Hermann mentions gonorrhœal erythema exudativum and nodosum; Cassal saw an abscess of the skin with gonorrhœal suppuration in a child eleven years old suffering from multiple gonorrhœal arthritis.

The **diagnosis** is easy if we call to mind the possibility of the gonorrhœal nature of the joint affections. In no case of polyarthritis must the examination of the conjunctivæ, the vulva, or the male urethra, be neglected. Features distinguishing it from acute articular rheumatism are the symptoms of an inflammation usually of greater intensity, a longer duration of the localization in single joints, also relatively the monarticular localization, the rarer complication of endocarditis, and finally the poor results of salicylate therapy. In doubtful cases the proof of the presence of gonococci in the joint effusion (which by the way is not always successful) must decide.

The **treatment** brings results. Enveloping with cotton wadding and fixation of the joints generally suffices. With children beyond the nursing age a trial with sodium salicylate is at least advisable.

Hermann records a prompt result after an intravenous injection of collargol [3.0 c.c. (ɱ 45) of a 2 per cent. solution for a fourteen-year-old boy]. In severe cases it would be well to take this method of treatment into consideration. Exceptionally it may become necessary to resort to arthrotomy (Paulsen). Of especial importance is a thorough removal of the source of gonococcus infection.

SCARLATINAL POLYARTHRITIS

Inflammation of the joints occasionally develops in the course of scarlet fever, which may greatly resemble acute articular rheumatism. Generally it appears the second or third week of the disease, or possibly sooner, and it may completely vanish in 6 to 10 days. Most frequently the wrist-joints are affected symmetrically, then those of the shoulders, knees and feet. As a sequel to scarlet fever, endocarditis and affections of the joints may be combined. Even without salicylate treatment these cases of arthritis are apt to yield to envelopment with cotton wadding and immobilization. This differs from the purulent joint inflammations which occur in scarlet fever as a result of streptococcic sepsis, and which require surgical treatment.

PNEUMOCOCCIC ARTHRITIS

Pneumococcic arthritis which has only recently received proper attention owing to the labors of Pfisterer and Herzog, deserves special mention in these pages, since it is apt to occur in childhood, particularly in the first and second years of life. Bronchitis or pneumonia may or may not precede the arthritis. The pharynx and middle ear may be considered as portals of entrance. Now and then pneumonia follows the joint disease.

The **pathology** is one of suppurative effusion, with a copious infiltration of the capsule, which like the pus is permeated with diplococci positive to Gram's stain, while the cartilage shows little or no noticeable change. The affection is usually monarticular, sometimes oligarticular. The most frequently involved areas are the shoulder, knee, or hip. It is rare to have a true septic course in which many joints participate and lead to death. Complications with meningitis, empyema and peritonitis often occur (Hagenbach, Römheld). Epiphyseal osteomyelitis may exist at the same time and perhaps be taken as the primary cause of the joint suppuration (Herzog).

Diagnostic Signs.—Characteristic symptoms are great swelling and widespread inflammatory œdema, with simultaneous pallor of the skin. Notwithstanding the severe local manifestations and the high fever the general physical condition and sleep are proportionately only slightly impaired.

The **differential diagnosis** from articular rheumatism and tuber-

culous coxitis, requires no discussion; however, there is greater probability that pneumococcus arthritis will be confounded with gonorrhœal arthritis. Aside from the primary sources of infection, which can be etiologically proven, it is necessary in all suspicious cases for the verification of the diagnosis in pneumococcic arthritis to make as soon as possible an exploratory puncture. The lancet shaped Gram-positive capsulated diplococci are easily identified under the microscope. Culture and animal inoculation may be of service for positive identification.

The **prognosis** is unfavorable if the arthritis is only a local manifestation of a severe general infection; otherwise it depends essentially upon a timely diagnosis and incision. Thick creamy pus gives a better outlook than a thin pus. The curative result is, as a rule, functionally perfect.

As far as therapeutics is concerned, only the earliest and sufficient incision is to be considered. Expectant treatment or puncture are positively to be rejected.

HEREDITARY SYPHILITIC ARTHRITIS

As a consequence of hereditary syphilis, arthritis appears as a belated manifestation in children who have not been specifically treated. The recognition of these cases, for which we are principally indebted to ophthalmologists, is all the more important because antisyphilitic treatment (specifically with iodide) generally results in a complete and rapid cure. Less frequently in children under five (more frequently in those between six and ten years) there arises without any traumatism, either subacutely or chronically an effusion into the joints, which may become very copious, causing at the same time surprisingly little subjective disturbance. Puncture shows serofibrinous fluid. Temperature is normal or subnormal. Cases of severe inflammation, however, accompanied by high fever also accur (Bosse). The knee-joints are most frequently attacked, and the disease almost always affects both of them in the course of time. Therefore, every case of gonitis (inflammation of the knee-joints) beginning in the manner described (and especially if the second knee begins to be involved in the same way), will cause us to suspect secondary syphilis. It will then be necessary to explore the family history of the child as well as its physical condition.

Should parenchymatous keratitis be present along with the articular affection, it will more easily verify the diagnosis, unless the same conclusion has been reached by treatment for syphilis previously employed. It is usual for hereditary syphilitic arthritis to be combined with parenchymatous keratitis. The arthritis precedes the eye affection almost always by months or years.

Bosse found arthritis of an hereditary syphilitic nature in 37 per cent., von Hippel in 56 per cent. of all cases of parenchymatous keratitis.

The **treatment** is dependent on the diagnosis. The specific treatment is generally successful even in cases accompanied with high fever and inflammatory signs which appear to require surgical procedure.

CHRONIC ARTICULAR RHEUMATISM

By chronic articular rheumatism, we understand a series of types of diseases, etiologically and clinically not quite alike; for the present, a strict classification does not appear advisable. The cases, taken all in all, are rare. (About one hundred have been reported in the literature.) In some countries, *e.g.*, England, they seem to be more frequent. In childhood, too, we may distinguish two different types. Individual cases of course may present various deviations.

Fig. 111.

Secondary chronic arthritis following acute articular rheumatism. Girl nine years old. Acute articular rheumatism. At seven and a half years joint residuals, originally only in the joints of hands and feet. Progressive participation of the large and all the small joints of the extremities, and of the vertebral column, partly accompanied by attacks of pain. Insufficiency and stenosis of the mitral and tricuspid valves. Epileptic attacks; chronic pachymeningitis, encephalitis (of a rheumatic origin?) Death.

1. CASES COMPLICATING ACUTE ARTICULAR RHEUMATISM

Group (*a*). Those gradually arising in the course of a greater number of single acute attacks (secondary chronic arthritis), in which at first only slight joint disturbances remain, but become worse with every new attack and spread to other joints. This is in general the mildest form so far as prognosis is concerned (Fig. 111).

Group (*b*). Developing directly from the first acute attack, without the occurrence of even a temporary return of symptoms. From the very beginning these cases are characterized by their unusual localization or peculiar course (Heubner) in that the disease attacks preferably the small finger-joints with co-participation of the temporomaxillary and sternoclavicular joints, the symphyses, etc. Disease of the cervical portion of the vertebral column especially may initiate such cases; and furthermore the salicylate often proves to be partly or altogether ineffectual (Figs. 112 and 112*a*). These cases of the first group often appear in combination with endo- and pericarditis and they show, starting from the large joints, a centrifugal progression in the involvement of the joints. Here might be added those rare cases of chronic articular

rheumatism which pursue a similar course as sequels to the acute infectious diseases (influenza, scarlet fever, measles, see Fig. 113).

2. CASES OF PRIMARY CHRONIC ARTHRITIS

The disease begins subacutely or chronically, without or attended by more or less severe attacks of pain, and may run a subfebrile course. Centripetal progression starts from the small finger- or toe-joints. Sometimes the knee and elbow may have been previously attacked. Endocarditis is only exceptionally noticed.

Fig. 112.

Secondary chronic arthritis following acute articular rheumatism in the second year of life. Girl seven years old. Swelling and immobility of all the joints of the extremities, with participation of the dorsal and cervical portions of the vertebræ. High grade muscular atrophy; endocarditis.

Of sixty-six cases I found the beginning of the disease mentioned in twenty-seven individuals, in the first to the fifth year of life (two of them in the first, eight in the second, ten in the third, fourteen in the fourth), twenty-two in the six to the tenth, seven in the eleventh to the fourteenth year.

The *articular changes* themselves cannot be strictly distinguished clinically or anatomically in either type. In general, there is at first an effusion or a doughy swelling; later on more marked changes in the capsular ligaments and the surrounding soft parts (villous proliferation, contraction of ligaments) in consequence of which there is a decided impediment to motion, finally positive contractions and immobilization, resulting in fibrous adhesions and production of ankylosis together with erosion and connective tissue transformation of the articular cartilages. Further, and usually later development shows participation of the bones, changing them into the types which cannot be distinguished from the so-called deformative joint processes. Separations of the epiphyses likewise occur (Spitzy).

PLATE 25.

a. Chronic progressive polyarthritis. Taken from a ten-year-old girl who had had the disease for eight years. The phalanges are thickened, especially the middle ones. The contraction of the capsule presses the surfaces of the joints close together and they appear shorter and wider. The fingers are slightly bent, the little finger most noticeably. The carpal bones are forced together by the contraction of the capsule and ligaments. There is no secondary growth of bone, which is characteristic of arthritis deformans.

b. Radiograph of a normal hand. A comparison with a normal hand shows the typical changes in chronic progressive polyarthritis.

From a clinical standpoint, the nodular swelling of the finger-joints is particularly striking (Figs. 112*a*, 114, 114*a*, *b*, *c*). The skin from time to time assumes a glazy inflamed appearance. Deviations of the fingers or toes to the ulnar side do not seem to occur in childhood, but another kind are seen.

Certain localizations, quite frequent in the chronic forms, are apt to put the poor suffering patient into a most lamentable state. This is also the case where the vertebral column is affected, particularly the cervical portion, and sometimes in the temporomaxillary and costal articulations.

Fig. 112 represents a girl in the pagoda attitude, with almost complete immobilization; only movements of the knees and slight motion of the arms were possible, the hips and the head were nearly immovable. She could lie only on her side.

The symmetrical attack of both halves of the body is extremely persistent and this gave rise to the opinion that the entire affection is to be regarded as a tropho-neurosis. In some cases, however, this symmetry is not well marked. Atmospheric changes may bring on an aggravation of pain, passive motion sometimes elicits marked crepitation, particularly if the immobility in the stiffened joints is diminishing. Extreme atrophy of the muscles surrounding the joint is very noticeable in all severe cases, produced partially by inactivity, partially through reflex tropho-neurotic influences (Hoffa).

Fig. 112*a*.

Secondary chronic arthritis following acute articular rheumatism. The same child as in Fig. 111. Swelling of the wrist-joint, back of the hand and all the small finger-joints.

The extremities assume with the thickening in the joints, quite a characteristic appearance (see Fig. 112).

The diminution of the bone at the diaphysis is in part due to a high grade concentric atrophy of the bones themselves (Johannessen, Kienböck, Reiner). The X-ray pictures show a continuous interstitial atrophy of the bones involved. An unusual diagnosis by means of the X-rays is reported by Reiner, namely, a corroded or split appearance of the badly swollen epiphyses of the phalanges of the fingers.

The children for the most part show a moist anæmic skin, once in a

while, profuse perspiration with a miliary eruption, especially in primary cases, followed in one of my cases by furunculosis. Generally there is no fever, but it is more apt to occur in the primary cases.

Endocarditis with valvular lesions is found only in cases of the first group (see above).

Rare occurrences are abnormal lengthening and thickening of the large toe (Johannessen, Spitzy), diminution and lessening of the lower jaw (Diamantberger), prevention of the growth and development of all the extremities (Hoppe-Seyler) and exophthalmos (Diamantberger). Only one case belonging to the first type, that of Henoch, exhibited rheumatic nodules.

Fig. 113.

Secondary chronic arthritis following measles. Boy four years old. Hand-, knee- and ankle-joints swollen. Finger-joint unaffected. (Spitzy.)

A specific type not yet explained as to its nosological value, is represented by *Still's disease*. Here is found an almost painless chronic thickening and stiffening of the joints of little children, accompanied by fever, either continuous or periodical. The disease, beginning with the knee-joint, wrists, or the cervical portion of the vertebral column, gradually attacks the ankles, elbows and fingers, without leading to any destructive articular transformations. There is no endocarditis, but at the same time pericardial adhesions have been noticed. The most conspicuous manifestation is the hypertrophy of the spleen and the multiple swelling of the lymphatic glands. It yet remains an open question, whether or not these cases are possibly due to tuberculosis or to chronic sepsis.

Course and Termination.—The course of the affliction is chronic in the extreme, and may extend into years and eventually decades. At any rate the affection advances in children with greater rapidity than in adults. Long intermissions occur. Recovery or at least considerable improvement is seen especially in cases of the first group. Improvement is found also in very rare cases, of course, in children of the second group. Death is either the result of general exhaustion or of a secondary tuberculosis.

Diagnosis.—The differential diagnosis should present no difficulties except to exclude syphilis and tuberculosis. Regarding the former we refer to its proper section. Multiple fungous joint disease may produce an appearance which is very similar to chronic rheumatism; here, however, tuberculous disease of the bones is often found, a fact which is proven by the X-ray pictures.

Since secondary tuberculosis occurs frequently in cases of real chronic articular rheumatism, it would not be reasonable to draw comprehensive conclusions, either from the tuberculosis of the internal organs, or from a positive tuberculin reaction. Greater weight should be attributed to a positive result from intra-peritoneal inoculation of a guinea-pig with the synovial fluid obtained by puncture, although even a secondary tubercular infection might have to be considered.

How far the presentation of this disease, "Rhumatisme tuberculeux" by the French (Bérard and Destot, Barjon, Poncet, Maillard) is consistent with the facts, only further investigations will show. Furthermore, it may be mentioned that hæmophilia in connection with articular hæmorrhage may result in a chronic arthropathy, which might remind one of chronic rheumatism. Arthritis urica is so rare in children that we may forego discussing it here. Whether it will be possible to eliminate clinically from chronic articular rheumatism, synovitis chronica villosa, as described by Schüller (a disease which is said to originate from a special cone-shaped bacillus) will have to be determined only by further investigations.

FIG. 114.

Primary chronic arthritis (rhumatisme nouveux). Boy four years old. Nodular swellings of the finger-joints. Swelling of the hand-, knee- and ankle-joints. Participation of the left hip-joint. Beginning of disease in the third year. (Spitzy.)

Prophylaxis.—Etiologically only two really effective factors are known to us; namely, rheumatic heredity and the influence of damp and cold habitations. The essential points to consider, therefore, against the further development of the disease in children afflicted with rheumatism are hygienic precautions in the dwelling and proper clothing, as well as appropriately guarding the child against inclement weather.

Treatment.—Only cases of the first group are amenable to treatment with the salicylates, as aspirin, etc., and in cases of intercurrent acute attacks it will be well to return to these remedies.

If the salicylates, however, are ineffective in an attack of acute articular rheumatism, at its very outset, and the disease shows a tendency

to assume a chronic course, then it is advisable to place the joints into a position of repose, and to use local applications of mesotan (see page 497).

Later it is well to start with what is paramount to all other treatment, *i.e.*, physical therapeutics; these procedures may sometimes be efficiently assisted by the quite persistent administration of iodide of sodium. After all, the most important mode of treatment, and one which must be adhered to with great patience, is gentle massage and careful passive motion. At the same time a local treatment with 10 per cent. ichthyol in vaseline may be useful. This is to be rubbed in at night and covered with wadding, next morning slight friction with French brandy.

FIG. 114a.

Primary chronic arthritis. Girl one and a half years old. Nodular swelling of the joints of the hands and feet. Onset in the right elbow-joint.

Immobilizing bandages ought to be avoided as far as possible except in cases of acute exacerbations. In advanced stages of the disease the production of active or passive hyperæmia proves useful. Bier's process of producing congestion (stasis), or preferably hot air or electric light baths may be considered.

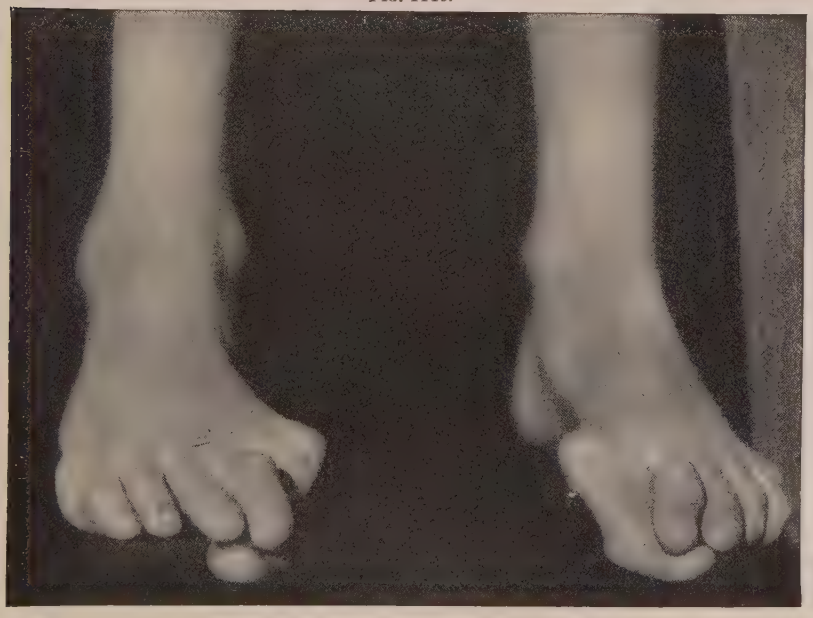
Very favorable but of course only temporary results have been observed from the use of daily hot sand baths at 30–35° C. (86–95° F.); for one half to one hour. Occasionally applications of fango (fango poultices) of 40° C. (104° F.) daily around the joints for six hours have attained some success. Frequent very warm applications of such poultices to the vertebral column occasionally lead to excellent results. As alternatives douches deserve consideration, if there is no tendency toward acute relapses. Some French authors have seen results with the galvanic current. In conjunction with external treatment, an internal or subcutaneous treatment with arsenic may be tried. Occasionally rectal feeding may be necessary if there is a marked involvement of the temporomaxillary articulation.

As to the success of hydrotherapy (as Nauheim, Teplitz, Wildbad, etc.) we can hardly judge, since almost without exception only children of the poorer, or the poorest, classes are afflicted with the disease. If stiffness of the joints and contractures have already formed, then very beneficial functional results can be obtained by orthopedic and mechani-

Fig. 114*b*.

Arthritis deformans in an eight-year-old girl.

Fig. 114*c*.



Arthritis deformans in a twelve-year-old boy.

cal treatment, reduction, tenotomy, plastic surgery of tendons, traction, and apparatus (Spitzy, Reiner).

Possibly thiosinamin could be used in these cases to great advantage, although so far as I know, it has never been tried, in spite of its softening influence upon the cicatricial and connective tissues, especially as a transition from the chronic into an acute inflammation would be welcomed.

Menzer's serum has not as yet been tried. The hypnotic suggestive therapeutic endeavors of some authors (Bernheim, Grossmann) can be regarded only with skepticism especially with children.

A special surgical procedure, *i.e.*, injection of iodoform guaiaco glycerin emulsion, or a free opening of the joints and excision of the villous coat, would have to be considered in a case of Schüller's synovitis chronica villosa.

Von Starck saw rapid improvement result from inunctions of ungt. Credé in a case presenting the picture of Still's disease. In cases attended with fever, the use of colloidal silver in the form of Credé's ointment or intravenous collargol injections would, at any rate, be worth a trial.

MALARIA *

BY

DR. HENRY L. K. SHAW, OF ALBANY, N. Y.

MALARIA may be defined as an infectious disease due to the presence in the blood of a parasite called hæmatocytozoön malariæ. It is characterized by paroxysms of intermittent fever with enlargement of the spleen.

Etiology.—Laveran discovered the specific organism of malaria in 1880. It is an animal parasite belonging to the group of protozoa and attacks the red blood cells and for this reason is called a hæmacytozoön. There are three forms of the parasite, namely: tertian, quartan and the æstivo-autumnal.

1. The tertian parasite completes its cycle of development in the human body in forty-eight hours. A double infection with the tertian parasite is common in children and is called the quotidian type of fever. When first seen it is a small oval particle within a red blood cell. This develops rapidly and in a few hours pigment may be seen around the periphery of the parasite. There is distinct amœboid movement, protrusions being put forth and then withdrawn. The hæmoglobin in the red cells fades while the pigment in the parasite increases. Just before the chill the parasite fills most of the red cells. Segmentation now takes place and the segments or spore forms are freed in the blood stream and are ready to attack new red cells and go through another cycle of development.

2. The quartan type is rare in the United States and takes seventy-two hours to complete its cycle of development and the chill and fever are seen on every fourth day.

The early stages are like the tertian but on the third day the parasite is quite still and the pigment is at the periphery.

3. The æstivo-autumnal variety is found in the more irregular fevers. It takes from twenty-four to forty-eight hours to complete its cycle and curious crescentic forms are seen after a week. There is but little pigment.

It is now definitely established that the parasite enters the blood through the bite of certain forms of mosquito. The mosquito is the intermediate host and two days after the mosquito has bitten the person whose blood contains the malaria parasite small refractive bodies may be

* The German editors did not include an article on malaria. In order to meet the requirements of the American physician this article has been included in the American edition (H. L. K. S.).

seen in the stomach of the mosquito. Later, these burst into myriads of spindle-shaped sporozoids and get into the salivary glands of the mosquito and thence infect the person bitten.

The parasite is only carried by the mosquito of the genus anopheles. The most common mosquito is of the genus culex. The two have distinctive characteristics. The anopheles has two large palpi, one on either side of the proboscis, and mottled wings. The harmless culex has small palpi and no spots on its wings. The anopheles, when on the wall or ceiling, holds its body away from the wall at an angle of 45 degrees or more, while the culex holds its body parallel to the wall and usually the two hind legs are crossed over the back.

Malaria is endemic in certain localities. The rôle of the mosquito shows the reason for the liability to contract malaria after sunset, the danger from stagnant pools and marshes, the susceptibility of infants and young children and the greater frequency in the spring and summer.

Pathology.—In mild cases of malaria there is little alteration in the structures of the body besides the changes in the blood and an enlarged spleen. Fatal cases are very rare in infants and children in this country.

In the severer and pernicious forms both the liver and spleen are enlarged and pigmented.

Symptoms.—The symptoms are apt to be most irregular and obscure in infants and young children. The typical adult types are found in children over six years of age.

Vomiting, chilly sensations and not infrequently a convulsion may usher in an attack. Distinct chills are not often seen in young children. They are replaced by cold hands and feet, blue lips and nails and drowsiness.

The quotidian type is the most common form although the tertian is not infrequent. The quartan and æstivo-autumnal are very rare in the United States.

The fever is relatively higher than in adults and may reach 106° F. After from a half hour to four or five hours or longer the fever breaks and gradually falls to normal or below. The sweating stage is only slightly marked and may be entirely absent. When the fever falls the child feels weak but soon feels as well as usual. The child will feel well until the second paroxysm occurs. This is not so well marked as the first and the following ones even less so.

Irregular or masked forms are more frequent in young children and are more apt to be misinterpreted.

The child may have no paroxysm at all and the fever may be very irregular in type, simulating many diseases. Headache is very frequent and may be associated with vertigo and drowsiness. Pain in various parts of the body is not uncommon.

Holt called attention to acute pulmonary congestion which may accompany the paroxysm of malaria. This may give rise to obscure

symptoms. The onset is acute with vomiting and prostration, high fever, cough, rapid respiration and often slight cyanosis. Feeble respiration is heard over one or both lungs occasionally with moist rales. These symptoms may disappear in the course of a few hours to return with the next paroxysm. If quinine is given they may entirely disappear.

Chronic Forms of Malaria; Malarial Cachexia.—These cases are often mistaken for anæmia and the real cause overlooked.

The child is pale and sallow and the spleen is enlarged. There may be a slight irregular fever. There may be slight œdema of the lower extremities, general muscular weakness, coated tongue and loss of appetite. There is liable to be indigestion with attacks of vomiting. There is a tendency to hæmorrhage and the urine may contain blood. The only positive evidence of malaria in such cases is the presence of the malarial organisms in the blood.

Diagnosis.—A positive diagnosis is made by an examination of the blood. It requires, however, considerable practice to become expert in the diagnosis of malaria from blood slides. Both stained and fresh specimens should be examined. The best time to take a specimen of the blood is a few hours before the paroxysm, before quinine has been administered. If malaria is suspected repeated examination of the blood should be made. The therapeutic test with quinine may be made in cases where a blood examination is not feasible. A fever that reacts promptly to quinine is probably malaria and one that does not is due to some other cause.

The periodicity in the symptoms is suggestive of malaria as is an enlargement of the spleen. The spleen is enlarged in a child when it can be felt below the border of the ribs. Malaria must be differentiated from typhoid, tuberculosis, septicæmia, broncho-pneumonia and certain forms of nephritis.

The recurring chills and fever in pyelitis are often attributed to malaria. Conditions accompanied by an enlarged spleen such as anæmia, syphilis and rickets may be mistaken for malaria.

With the modern methods of diagnosis no physician should fall into the error of regarding all vague and indefinite symptoms as malarial.

Prognosis.—Malaria is rarely fatal in young children, but it may lower the child's resistance so that he is more liable to succumb to some acute disease.

Treatment: Prophylactic.—This consists in malarious districts in destroying mosquitoes and in protecting children from their bites. Drainage of marsh lands and the use of crude oil on the breeding places are efficient. The windows, doors, porch and the baby's crib should be well protected with screens and mosquito netting. Ointments containing pennyroyal, turpentine, etc., may be used on exposed portions of the body.

Therapeutic.—The general treatment is symptomatic along general lines. An initial purge with calomel is indicated. During the chill, stimulants or a cold bath may be required and in the hot stage, ice to the head and frequent sponging.

The specific drug is quinine. This should be given early and continued until a cure is effected. The bisulphate in solution is preferable in young infants. Relatively larger doses are required for infants and young children than for adults. An infant one year old will require from 10 to 15 grains of the bisulphate in twenty-four hours and even larger doses may be given without producing cerebral symptoms.

When the quinine can not be tolerated by the stomach it can be given in solution per rectum through a catheter. Suppositories of quinine are sometimes used. The hypodermic injection of the hydrobromate or bimuriate of quinine is advocated by some but it should only be employed in serious attacks, on account of its producing local irritation and abscesses.

In children over a year old the taste must be disguised. Euquinine and tannate of quinine are almost tasteless. There are several preparations of quinine combined with chocolate on the market. An aqueous solution of the bisulphate can be mixed with the syrup of red raspberry, sarsaparilla, etc. Capsules or wafers containing the sulphate of quinine can be given to older children.

In young children it is best to give the quinine in frequent small doses. The quinine should be given for at least a week after the last symptom of malaria.

In chronic cases iron and arsenic in some form should be given.

SYPHILIS

BY
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The chapter on Syphilis of Children will be devoted to a discussion of all those changes brought about by syphilis that affect the human organism from the time of conception to the beginning of puberty.

Syphilis in childhood may have its origin in an hereditary transmission from diseased parents, or it may be acquired as an ordinary infection through contagion. One must, therefore, distinguish between hereditary and acquired syphilis.

HEREDITARY SYPHILIS

1. THEORETICAL CONSIDERATION OF THE HEREDITARY TRANSMISSION OF SYPHILIS

In acquired infantile syphilis there is a single mode of infection just as in later years, *i.e.*, contact infection; hereditary syphilis on the other hand may be transmitted in two ways. We may have a germinal hereditary transmission through the germ-cells, or a direct intra-uterine infection. Ever since Kassowitz's epoch-making work on this subject (1876), the possibility of a germinal transmission has been undisputed, while intra-uterine infection by way of the placenta was held to play a subordinate part. Recently Matzenauer (1903), as Oedmansson did formerly, has maintained that a transmission from the spermatozoa to the ovum has not been proven, and that intra-uterine infection is the only conceivable method of transmission of syphilis from the parent to the offspring. He supports this view by the fact that a purely germinal transmission is unknown in any other infectious disease. His main thesis is: "Without maternal syphilis, there is no hereditary transmission of the disease of the child."

It is not possible in a work of this kind to discuss this view in detail: a view that would have at least the advantage of greater simplicity if it were tenable. I, for my own part, must hold to the possibility of a purely paternal, *i.e.*, spermatic, transmission of syphilis, a conclusion that is based on many years of careful observation. With all due

respect to Matzenauer's attempt to simplify this complex question of hereditary transmission of syphilis I cannot refrain from expressing my conviction, that in his zealous endeavor to refer all questions pertaining to hereditary syphilis to intra-uterine infection by way of the placenta, he has, in more than one way, distorted clinical facts. With the large and constantly increasing literature on the subject of hereditary syphilis, it is impossible to go into details and mention all of the past and present authorities, and their various views. It will be possible to take only a general survey of the most important views and questions bearing upon the subject. As to terminology, Solger and Martius maintain that if Matzenauer's view were accepted, the term "hereditary syphilis" would be incorrect, and "congenital syphilis" should be put in its place, since only such disturbances could be looked upon as hereditary, as had been transmitted through the germ. Schaudinn, in conjunction with Hoffman, has possibly found the specific cause of syphilis in their *spirochæte pallida*. The demonstration of this bacterium, that is characterized by a special form with narrow, steep, and numerous convolutions (up to 14), is most satisfactorily made by staining with a modified Giemsa stain dried specimens obtained from the tissue juices of eroded syphilitic primary and secondary lesions. Buschke and Fischer, Hoffmann, Levaditi, Salomon, Leiner, Nobécourt, Bayet, have all found the characteristic spirilla in the contents of the blebs of syphilitic pemphigus. M. Oppenheim and O. Sachs, however, could not find them in the same lesion. In the liver, spleen, lungs, lymphatic glands (Bertarelli and Volpino, Brönnum, Ellermann, Reischauer, Buschke, W. Fischer), and in the blood of children with hereditary syphilis, this parasite has been seen, so that Levaditi considers hereditary syphilis as a spirillosis. The frequent positive findings in hereditary syphilis, and the occurrence of spirochæte pallida in the inoculation scleroses of monkeys, would lead one to attribute to this parasite a more important rôle in the etiology of syphilis, than to the other microörganisms that have been advanced as the specific cause of this disease.

Classification of Hereditary Syphilis.—Two factors must be considered in the hereditary transmission of syphilis:

1. The hereditary transmission of the contagion, which leads to genuine, virulent infection in the offspring.

2. The hereditary transmission of certain constitutional changes that have been brought about in the parent by the specific poison, these changes manifesting themselves in the offspring as more or less well marked general disturbances such as one finds in the offspring of alcoholics, arthritics, etc.

Those belonging to the first group represent congenital syphilis in the narrower sense. This may be divided into syphilis that has manifested itself during intra-uterine life, and that which has appeared only

post-partum. The former may be subdivided into syphilis embryonalis, fœtalis, and neonatorum. The latter, according to the views of many, should be subdivided into syphilis congenita præcox and tarda, depending upon whether the congenital disease first manifested itself shortly after birth, or not until the time of puberty. That the latter form has in no way been proven, may be stated in advance at this point. There is still less evidence of an inheritance of syphilis by the grandchild, *i.e.*, the third generation, which, if it did exist, would form a special form of late syphilis.

The second main group no longer depends upon changes brought about by direct hereditary transmission of germs, but upon the development of disease and of dystrophic conditions, such as arrest of development, and constitutional disturbances, which do not themselves represent syphilitic affections, but are connected with, and dependent upon, the depraving influence of syphilis upon the general health of the parents (A. Fournier's Parasyphilis). Similar symptoms may appear as a result of syphilitic infection, either congenital or acquired, later in life, so that besides the congenital parasyphilitic affections, one must distinguish also those which appear later in life.

Sources of Hereditary Syphilis.—Hereditary syphilis may orignate from the father, or from the mother, or from both at the same time.

1. Syphilis from the Father.—Syphilis of the child originating in the father without infecting the mother (recently denied by Matzenauer), depends upon spermatic infection of the ovule, and its occurrence is demonstrated by the fact that women can bear, in turn, syphilitic and healthy children, if they have become pregnant first by a man with latent syphilis, and then by a nonsyphilitic man. It is further demonstrated by the striking results of antisyphilitic treatment of the husband alone in families where a mother, who is free from syphilis, has given birth to syphilitic children. The treatment of the husband alone, nearly always suffices to keep the later offspring free from syphilis.

Although we are not familiar at the present time with the real nature of spermatic infection of the ovum, the fact that women who are permanently free from syphilis can give birth to syphilitic children, is absolutely undeniable and can only be explained by the hypothesis of a purely paternal transmission of syphilis.

According to the law of Colles and Baumés (1837 and 1840), a mother who was well at the time of conception acquires immunity against syphilis by being pregnant with a child that is syphilitic from its father. This immunity of the mother is frequently looked upon as an expression of infection of the mother through conception, and the disease itself, under these circumstances, is spoken of as conceptional syphilis (A. Fournier).

a

b

Onychia syphilitica. *a*, process of healing, *b*, healed.

Eruption on face in hereditary syphilis.

Eruption on palm of hand in hereditary syphilis.

According to A. Matzenauer, these immune mothers have become syphilitic through an undiscovered contact infection from a syphilitic husband, and for this reason alone are immune. Even if it is entirely possible that the primary manifestations should be overlooked, it would be inconceivable that there should be complete and lasting absence of all syphilitic symptoms for many decades in women that have remained untreated and have been observed by experienced physicians. I consider such mothers simply immune, but not syphilitic. (Observations in 4 of my own families.)

The direct paternal transmission of syphilis to the offspring, depending upon the degree of virulence, can manifest itself in death of the fœtus, or in evident syphilitic manifestations at birth, or after birth, or through certain parasyphilitic symptoms early or late in childhood.

2. Syphilis from the Mother.—Several possibilities, according to various authors, are here to be considered: The mother may have been syphilitic before impregnation (anteconceptional); or she may have been infected in consequence of impregnation (conceptional), or after impregnation, *i.e.*, during pregnancy (postconceptional).

(*a*) *Anteconceptional Syphilis.*—If the mother is syphilitic and the father is well, one might think, by analogy with spermatic syphilis, of an ovular syphilis, remembering however the possibility that the fœtal infection may have been transmitted during pregnancy through the placenta of the diseased mother to the fœtus. The view formerly advanced by Kassowitz, that the placenta constituted a barrier between mother and child through which the contagion of syphilis could not pass, has not shown itself to be tenable. When the placenta itself becomes diseased there is no longer any hindrance to fœtal infection along the placental route.

(*b*) *Conceptional Syphilis.*—This term is used by many authors to designate infection of a woman through impregnation by a syphilitic man, an occurrence that is wholly unproven and incapable of proof.

As a clinical expression of conceptional maternal syphilis, one might think, first of all, of the occurrence of secondary symptoms without primary lesion, several weeks after conception (early conceptional syphilis), in which cases, however, one could not exclude an unrecognized primary lesion following ordinary contact infection.

The advocates of conceptional maternal syphilis accept also the possibility of a late form, *i.e.*, syphilis appearing many years after conception in the mother in the form of tertiary manifestations (Tertiarisme d'Emblée, A. Fournier, Finger, von During, and others), a view even less demonstrable than that of an early conceptional syphilis.

(*c*) *Postconceptional Syphilis.*—The mother is infected during pregnancy. The fœtus may, or may not, become syphilitic. If the mother under such circumstances transmits her disease to the fœtus that was

primarily healthy, during pregnancy, then we have a real intra-uterine infection. If the mother acquires syphilis during the early periods of her pregnancy, between the second and the fifth months, then the chances are greater that the child will be infected within the uterus than if the mother acquires the disease during the second half of pregnancy. Maternal infection occurring during the last two months of pregnancy does not seem to be dangerous to the child. In general, one must remember that intra-uterine fœtal infection is by no means a necessary sequel to the postconceptional maternal syphilis, but rather a facultative one. It is certain that intra-uterine transmission of syphilis is preceded by a specific disease of the placenta which causes it to be permeable by the contagion of syphilis.

In a case observed by Oedmansson, congenital syphilis occurred in the child after infection of the mother at the beginning of the third month of pregnancy.

The consequences of maternal syphilis, other things being equal, are considered as more serious to the offspring than those of paternal origin. Intra-uterine fœtal death and severe congenital syphilis are said to be more frequent in the former than in the latter. And yet recent maternal syphilis acquired during pregnancy is very frequently without any influence upon the fœtus, so that a healthy child may be born in these circumstances. Such observations teach that the placenta is in very many cases a protecting filter against the contagion of syphilis, and only when is becomes diseased can intra-uterine fœtal infection take place.

3. Syphilis mixta.—Father and mother are both syphilitic before conception. The severity and certainty of infection of the child is here in proportion to the recentness of parental infection. The germinal impregnation method of infection unites with that of intra-uterine infection in a combined action on the fœtus. In this method of infection there can likewise occur in the child, on theoretical grounds, genuine virulent manifestations of syphilis and parasyphilitic dystrophies.

Immunity to Syphilis of Mother and Fœtus.—One sees very frequently children who were born to mothers that had recently become syphilitic, that are free from all evidence of syphilis and remain so, and on the other hand mothers who are healthy and remain free from syphilis and yet give birth to children that are severely syphilitic. In the latter case we have to do with a fœtus infected spermatically, while the mother escaped from a contact infection with the specific factor. In this manner the mother acquires a high degree of immunity against syphilis, so that she can usually nurse her own specifically infected baby with impunity, while a wet-nurse would invariably become infected by such a child, in accordance with the law of Colles and Baumés. Exceptions to this law, usually in primiparæ, doubtless do occur, in spite of the

protest of Matzenauer, and these can then serve as the crowning evidence in favor of the possibility of a purely paternal transmission of syphilis.

It remains to be decided whence this maternal immunity arises. A number of authors hold the view based on Colles' law that these mothers are syphilitic and consider the disease as either latent and due to contact, or as conceptional. Others again would by no means identify this immunity with latent syphilis and would explain this immunity of Colles' by assuming the transmission of immunizing substances (antitoxins) from a paternally syphilitic fœtus to the mother during pregnancy. These mothers would therefore be immune to syphilis without, however, being syphilitic.

Whether this immunity in mothers who remain free from the disease and yet give birth to congenitally syphilitic children is permanent, or temporary, remains undecided. Probably it is only transitory, but nearly always extends beyond the period of nursing. Even if the mother does not become infected later in life in spite of continued cohabitation with a syphilitic husband this by no means is proof of a permanent immunity. If after the period of nursing the child is properly treated and later in life is kept free from virulent manifestations, then there is no longer any opportunity for infection of the mother from the child. The husband, however, in such cases is usually long before this free from infectious products, and it would be making a false deduction to maintain that all mothers of paternally syphilitic children are immune throughout life simply because they remain free from syphilis. In this view is found an answer to that objection to the existence of a pure Colles immunity which states that the action of antitoxins could give only a transient protection such as would follow vaccination.

Profeta's law attributes to the healthy child of a recently syphilitic mother immunity to syphilis and maintains that this immunity may even extend to all of the offspring of syphilitic parents. This view is not tenable since, as Matzenauer has rightly stated, a germinal transmission of immunity is unthinkable—children, born of syphilitic fathers, but of healthy mothers, that are healthy and not immune, cannot for this reason in any way be considered as exceptions to Profeta's law. This law has nothing approximating the authority of the law of Baumés and Colles, and all the less so since undoubted cases of syphilitic reinfection of congenitally syphilitic individuals are known (Hochsinger, E. Lang, von Düring, Tschlenow, etc.).

Since, in these children remaining free from syphilis yet born to syphilitic mothers, we have a transmission of soluble immunizing substances from the diseased mother to the healthy fœtus by way of the placenta, just as in the case of healthy mothers of paternally syphilitic children, it is impossible to assume a lifelong immunity. In both cases the degree of protection depends upon the duration and the amount of

the action of the antitoxin under consideration. Regarded from this standpoint the exceptions to Colles' law as well as to Profeta's law, are in no way surprising, indeed from a theoretical standpoint such exceptions are to be expected.

Hereditary Transmissibility.—In general, the ability to transmit syphilis to the offspring is proportional to the ability to produce contact infection, *i.e.*, contagion. It is essentially associated with the secondary stage, but by no means does it always follow, and in the tertiary stage only rarely so.

The general rule laid down by Kassowitz that the degree of transmissibility of syphilis gradually diminishes in proportion to the duration of the disease, remains, on the whole, correct, even if there are exceptions. In syphilitic families one sees as a rule first abortions, then stillbirths, then living premature infants, then living syphilitic infants, then living infants free from syphilis or not manifesting symptoms till after birth, and finally children that remain free from syphilis. To this rule one finds many exceptions, as the birth of healthy children in the midst of those that are syphilitic. This is spoken of as alternating transmission, and is considered by Matzenauer as one of the proofs of a purely maternal transmission.

The severity of the disease in the child depends upon the nature and manner of acquiring it and the time at which it occurs in the beforementioned scale. Children that are only slightly diseased often are born apparently well and do not give evidence of syphilis until some time during the first three months. When both parents are syphilitic, we have the conditions that most frequently lead to manifestations in the child, according to Fournier in 92 per cent. of cases. In purely maternal syphilis this occurs in 84 per cent. of cases according to Fournier, and in purely paternal syphilis, in 37 per cent. of cases.

In 72 marriages of fathers who were syphilitic and mothers who remained free from the disease, in the series of cases that I have observed, there were 110 stillbirths and 197 living infants. In 65 per cent. of the marriages in which the father alone was syphilitic there were stillbirths; in 35 per cent. there were living children only. In my series of 26 families in which there was positive maternal syphilis 19 mothers gave birth to 34 dead babies. According to my experience there is no essential difference as far as death of the fœtus is concerned between purely paternal and purely maternal transmission of syphilis. In 67 families, that I have observed, in which the parents were syphilitic there were 266 pregnancies; 142 children were born alive; 76 died during the first few days; and there were 48 abortions, making a total of 124 stillbirths in 266 pregnancies.

It is generally accepted that maternal syphilis loses its effect upon posterity less rapidly than that in which the father alone is affected, so

that a syphilitic woman who marries a second time and becomes pregnant by a healthy man, still frequently gives birth to infected children, and thus really transmits the disease from her first husband to the offspring to the second. Some authors claim to have seen transmission of syphilis in a virulent form more than twenty years after the mother was first infected.

With reference to the influence upon posterity of congenital syphilitics, one might think, from a theoretical standpoint according to Finger, of the transmission of genuine virulent manifestations of syphilis; of the production of parasyphilitic symptoms; and finally, of the occurrence of a congenital immunity to syphilis. The possibility of transmission to the third generation is wholly without proof. Its occurrence could be accepted as demonstrated only when a mother who is known to be congenitally syphilitic gives birth to a syphilitic child, while the father of the child is known to be free from syphilis, and the mother has not been specifically reinfected. Still less evidence is there in favor of the view frequently expressed that syphilis of the grandparents can produce dystrophy and immunity to the disease in the grandchildren, *i.e.*, in the third generation. In the whole consideration of whether syphilis can be transmitted to the third generation either in the form of genuine virulent syphilis, or as parasyphilitic manifestations, too little attention has been paid to the state of health of the second generation. Hereditary syphilis, in the first place, must be demonstrated in the second generation so as to leave no doubt; acquired syphilis, on the other hand, must be excluded with equal certainty, both as to infection in an individual previously well, and as to reinfection in one already congenitally syphilitic. The same naturally applies equally to the third generation.

2. FŒTAL SYPHILIS

In this chapter will be discused those changes brought about by the action of the transmitted syphilitic poison upon the fœtal organism, from the time of the formation of the ovum to the time of birth. There is here always the expression of severe infection of the fœtus caused by recent syphilis in the parents. The gravity of syphilitic manifestations in the fœtus is due to specific changes in the viscera, which changes are usually absent, or only slightly present, in those cases beginning after birth. In fœtal syphilis there is a striking affinity of the infectious material for the large glandular organs and for the growing portions of the osseous system, while the skin, which is a favorite place for an attack after birth is relatively immune before birth. There is developmental ground for this in that these organs which, at the time of the formation of the specific poison in the organism, show a peculiar hyperæmia, either functional, or associated with growth, take up the poison with especial avidity. If the contagion manifests itself in an early period

of fœtal life, then those internal glandular organs, the lungs, liver, kidneys and pancreas, that develop early are involved. Later, on account of the rapid growth in length of the fœtus, there appear changes at the epiphyseal borders in the hollow bones. The skin, on the other hand does not really develop its glandular apparatus till the later months of intra-uterine life, when it is preparing for its extra-uterine life, and so does not show characteristic changes till shortly before or after birth.

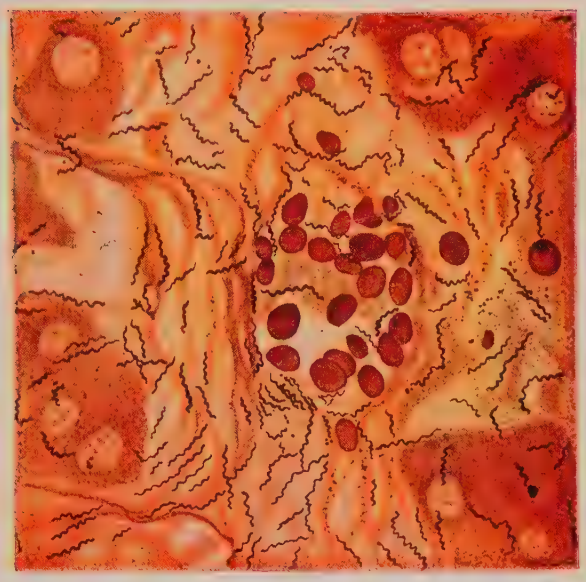
General Characteristics of Early Congenital Syphilis.—If one bears in mind the embryological conditions, it is a simple matter to find a satisfactory explanation of the genesis of the early lesions of hereditary syphilis. As opposed to acquired syphilis, the typical lesion of early hereditary syphilis is found in a diffuse cell proliferation having its origin in the perivascular connective tissue of the smallest vessels, *i.e.*, the mesenchyma. For this reason one very rarely sees a solitary syphiloma in the fœtus, or in the young infant, but rather, almost invariably, diffuse cell proliferation and inflammation.

It is a mistake to consider the visceral and bone changes of fœtuses and of newborn and young infants as tertiary, and the skin manifestations as secondary lesions, because they are identical with those occurring in these structures in acquired syphilis. The diffuse character of those lesions of early hereditary syphilis, no matter where localized speaks for a single uniform genesis, excluding the possibility of a division into secondary and tertiary lesions. The predilection of this inherited contagion as determined by embryological conditions, for those tissues that are especially characterized by marked vascularity and rapid growth during this period, speaks for the assumption that in the lesions of early congenital syphilis we have to do with a single, uniformly irritating action of the specific poisonous substance, which is earliest and most active wherever there is the greatest afflux of tissue juices. This has nothing in common with the usual classification of syphilis into stages.

The *anatomical picture* of the changes occurring in early congenital syphilis is an identical one in all organs. The most essential changes are found in the liver, lungs, kidneys, pancreas, spleen, thymus, and at the growing points in the bony system. Two kinds of lesions are most prominent:

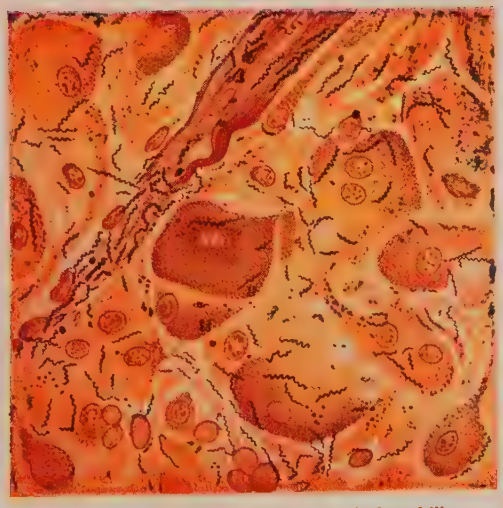
1. Diffuse cell proliferation, starting from the smallest blood vessels, in the interstitial connective tissue of these organs with a decided tendency to later contraction and to prominent participation on the part of the vascular system. In the small blood vessels this proliferating process begins in the outer walls in the form of a cuff and regularly advances peripherally toward the connective tissue, more rarely toward the inner wall of the vessels, frequently leading to obliteration (Fig.

Fig. 115*a*.



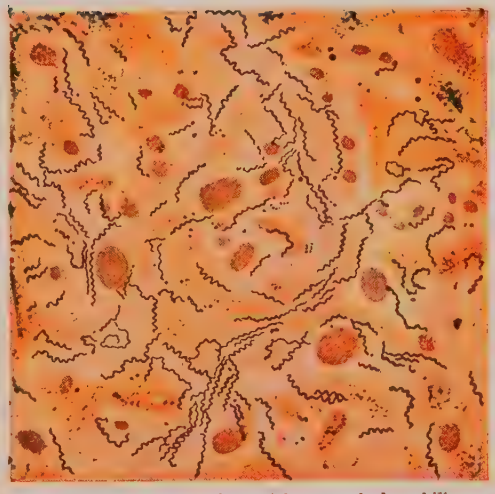
Suprarenal gland in newborn infant with congenital syphilis.

Fig. 115*b*.



Liver in newborn infant with congenital syphilis.

Fig. 115*c*.



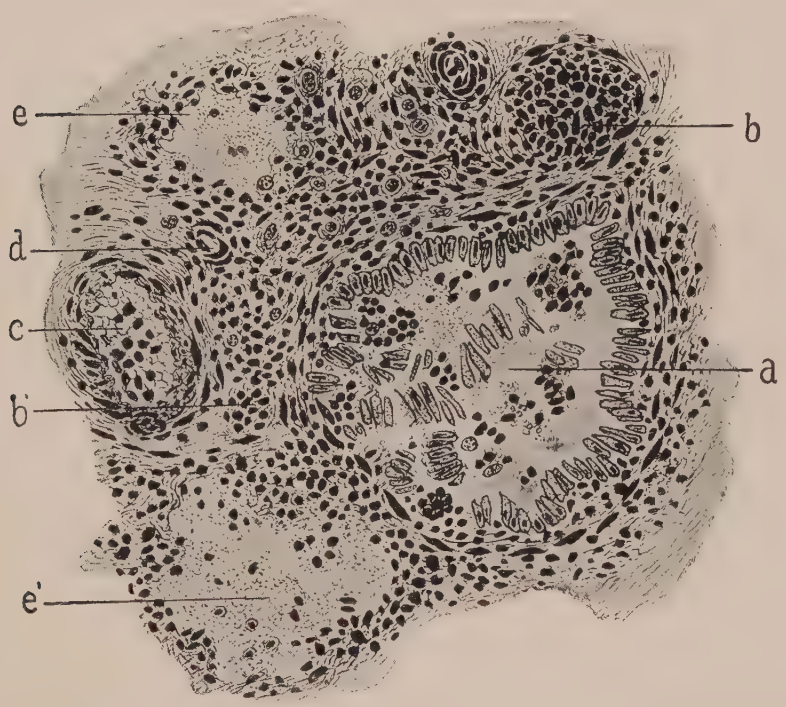
Spleen in newborn infant with congenital syphilis.

116). In the bone changes and in those of the skin we have an identical process, as will be shown later, although the conditions are not so evident at a glance as they are in the case of the viscera.

In all affected organs one may have localized denser collections of cells which are recognizable even macroscopically and are often spoken of as miliary syphilomata, but are not gummata.

This diffuse cell proliferation, or hypertrophy, of the mesenchyma which can so pervade whole organs of stillborn syphilitic infants that the

FIG. 116.



Lung of a syphilitic infant of the ninth month. White pneumonia. (*a*) A bronchus surrounded by diffusely infiltrated lung tissue and devoid of mucous membrane. The epithelium is in direct contact with the hyperplastic connective tissue. (*b' b*) Separated cylindrical epithelial cell fibres. Remains of fœtal epithelial tubules. (*c*) Larger blood vessels with diseased walls in the supporting tissue of the lungs. (*d*) Small arteries in infiltrated connective tissue. (*e' e*) Alveolar spaces packed with desquamated epithelium undergoing fatty degeneration and in part disintegrated, in part united into flattened masses.

parenchyma is no longer recognizable, was interpreted by Karvonen as a fœtal arrest of development of the mesenchmya and not as an inflammatory process involving the supporting tissue of the developing parenchyma, as Hecker and I teach. The same author, later Hecker, Terrier and Erdmann, pointed out the physiological richness in round cells of the fœtal parenchyma. Since, however, these organs in syphilitic fœtuses, in which the cell infiltration of the interstitial connective tissue is often a very extensive one, are heavier and larger than those that are not syphilitic, one cannot doubt that the pathological nature of this hyperplasia is that of an inflammatory proliferation.

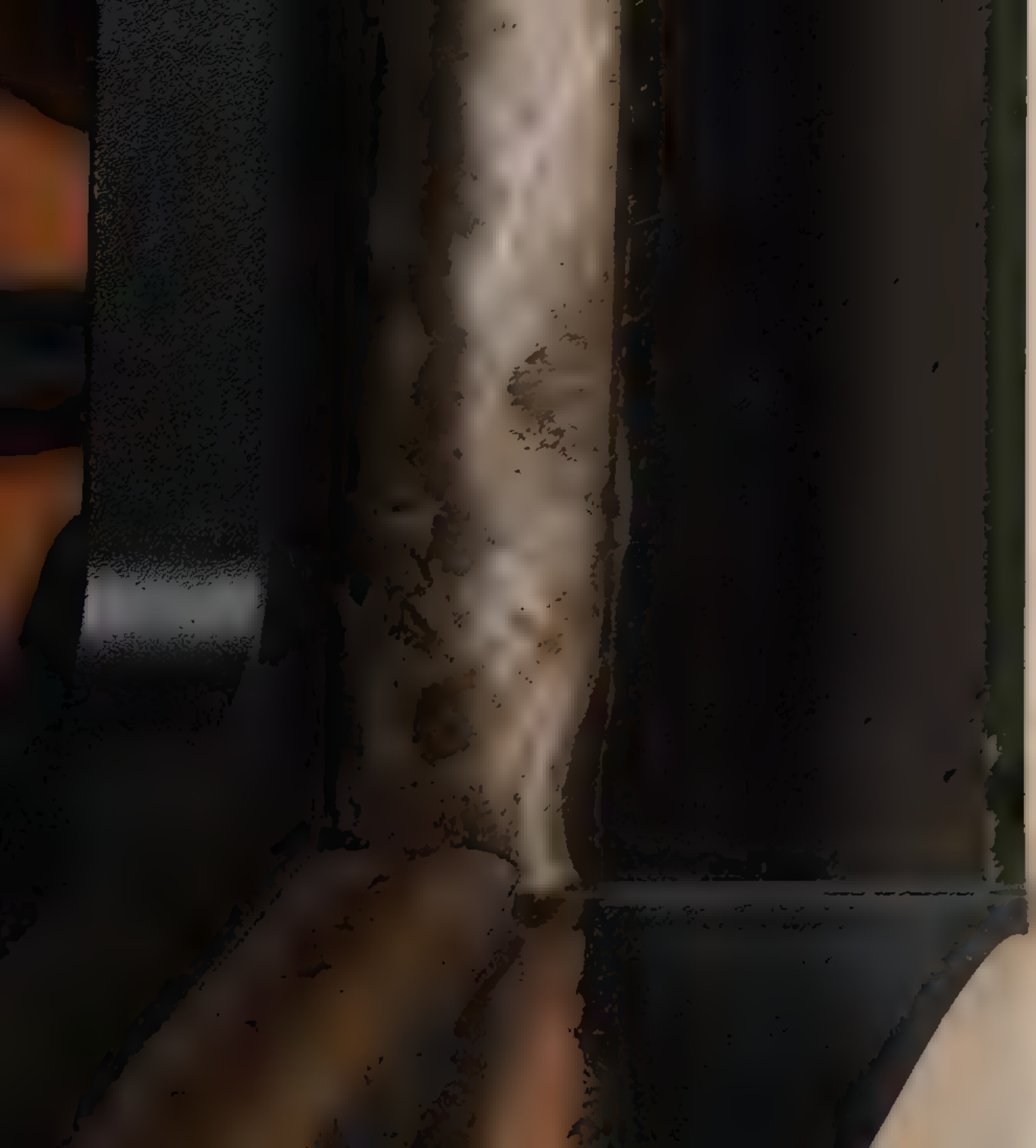
2. In the fœtal organs involved in this hyperplastic process there are characteristic and peculiar arrests of development of the parenchyma. Incomplete development of the Malpighian bodies, persistent epithelial ducts and the formation of cysts in the renal cortex, masses of epithelial cells that have been separated off and isolated, in the lungs, liver, kidneys, pancreas and gastro-intestinal tract and cyst formations lined with epithelium in the thymus may all be mentioned here. It is certain that the hyperplasia of the connective tissue areas goes hand in hand with a hypoplasia of the parenchyma. The growing osseous system of the fœtus and of the young infant shows similar disturbances of development.

Hereditary syphilitic changes of the visceral organs of fœtuses frequently are not demonstrable macroscopically. Only when we have circumscribed, focal collections of cell infiltration, and the formation of hard elevations, like callosities, is the diagnosis easy. At other times there is simply an increase of volume and consistency, most constantly in the liver and spleen, the weight of which as compared with the body weight is greater than normal in congenitally syphilitic fœtuses. The ratio of the weight of the liver to the weight of the fœtus is normally as 1:21.5, in syphilis as 1:14.7; that of the spleen is normally as 1:325, in syphilis neonatorum as 1: 198.

The liver of syphilitic fœtuses is always permeated by a large amount of interstitial cell infiltration, the dependence of which upon the vascular system is here very evident. One frequently finds in this organ which is usually very vascular, small yellowish masses from the size of a hemp-seed to that of the head of a pin, composed of cloudy and necrotic liver cells surrounded by inflammatory cells arranged about them as a focus. These are peculiar exudative formations that occur solely in early hereditary syphilis, and are to be interpreted as areas of anæmic necrosis. Very similar areas of necrosis are found in the kidneys, especially however in the suprarenal bodies, and also in the epiphyseal cartilages and in the cartilaginous ends of the bones of syphilitic dead born children.

More rarely there occur well developed sclerotic processes, *i.e.*, contractions in syphilis of the fœtal liver. An indurative enlargement of the spleen and pancreas is frequent. In the kidneys, besides the constant part taken by the vascular system in the form of a diffuse perivascular infiltration, there is practically always present an incomplete development of the cortical parenchyma with rudimentary development of the Malpighian bodies and of the tubular system.

The lung frequently shows characteristic changes that make it resemble sarcomatous tissue, due to the uniform infiltration with round lymphoid cells (Ziegler). Enclosed within these areas of interstitial cell infiltration are found remnants of fœtal lung tissue from a former



Frequently the cause of these early premature and still births is found in hydramnios resulting from an early phlebitis of the umbilical vein, which in turn is dependent upon specific changes in the placenta.

Changes in the placenta are regularly found in fœtal syphilis. The placenta is larger and heavier than normal. It is pale, has deformed lobes, is frequently yellowish in color, and the umbilical cord is hard and thickened. Histologically, the placental blood vessels show perivascular cell infiltration, and a pathological condition of the intima; the placental parenchyma shows, further, diffuse or nodular masses of cells and extensive foci of tissues that have undergone fatty degeneration. In the umbilical cord are frequently found perivascular infiltrations and characteristic changes in the blood vessels, on which alone the diagnosis of hereditary syphilis can be made if there is doubt otherwise as to the cause of fœtal death.

The living offspring of syphilitic parents, though they may show no clinical evidence of the disease, very frequently manifest constitutional inferiority as shown by general physical weakness. Among 48 syphilitic children born alive in Tarnier's clinic in 1900 and 1901 fourteen had a normal weight (not under 3250 grams), 38 an abnormally small weight, 15 of these weighing less than 2500 grams. The losses in weight of these fœtuses is the more striking, because they have regularly severe visceral affections which lead to an increase in weight of the larger glands (Hecker, Hochsinger).

In a few premature or full term infants characteristic changes are found in the skin and mucous membranes at birth. The most important skin lesion in this connection is syphilitic pemphigus. More rarely these children are born with a papular eruption. The most prominent congenital lesion of the mucous membranes is syphilitic coryza. Very frequently affections of the bones, of the eyes, and of the nervous system are present at birth, to say nothing of those that involve the liver, the spleen, the pancreas and the intestinal mucous membranes.

3. SYPHILIS IN INFANCY

Two kinds of organic changes are to be considered:

(*a*) Those that are carried over from the fœtal to the extra-uterine period, especially involvement of the viscera, of the osseous system and of the nose.

(*b*) Those that appear after a period of latency in infants apparently free from syphilis at birth, especially lesions of the skin and mucous membranes.

The period of *eruption* in hereditary syphilis deserves a brief general discussion in cases of the second group. There are children that are born free from syphilis from a clinical standpoint, that develop after several weeks or months an eruption similar to that occurring in acquired syphilis.

I II

I. Typical papular syphilide in hereditary syphilis.
II. Syphilitic papillæ on the tongue in an eight-year-old boy with hereditary syphilis.

The first appearance of this eruption is always during the first three months of life. Most frequently it starts between the second and sixth week after birth.

The first eruption is not always the first manifestation of the disease which may have appeared earlier in the form of specific lesions of the nose, viscera, or bones. In fact, the nose is nearly always involved before the skin eruptions appear. It must be remembered too that syphilis can run its course in infancy without any skin eruption whatever.

The most prominent symptom of infantile syphilis is found in a *rhinitis* that consists of an inflammation of the nasal mucous membrane, accompanied by hypertrophy. This very frequently begins during intrauterine life and is accompanied by disturbances of development of the skeleton of the nose.

My own material bearing upon this point comprises 256 cases of hereditary syphilis. I can recall no case in which this hyperplastic rhinitis was absent. Of 173 cases of specific coryza that are accurately described in my records, 65 can be used in determining the time at which this symptom first appeared.

In 38 cases the coryza was present at, or very shortly after birth.

In 5 cases it appeared one week, in 4 cases two weeks, in 4 cases three weeks, and in 2 cases four weeks, after birth. In 53 cases then it appeared during the first month, in the remaining 12 it occurred during the fifth, sixth and seventh weeks.

The affection begins with swelling of the nasal mucous membrane especially of the inferior turbinate bone. At first there is no secretion, but later there occurs a tough sanguinopurulent discharge with a tendency to the formation of crusts. There is a very characteristic snuffling sound later accompanied by a moist rattling sound due to mucus. This not infrequently permits the diagnosis of hereditary syphilis at a distance. This impeded nasal respiration makes nursing difficult, and the child frequently turns the head back and holds it in a position of opisthotonos in order to facilitate respiration.

This rhinitis may go no further than the stage of swelling, without any pus formation, or it may lead to ulceration and even to involvement of the cartilaginous and bony skeleton of the nose with resulting changes of shape of the external nose (see figures 120, 122, 132 and 133).

As a result of cicatricial contraction of the cartilaginous and soft portions we have, first of all, the pug nose. If the cartilaginous septum contracts completely a permanent deformity of the nose may result, so that the softer portion may form only a short projection beyond the bony portion with the nostrils directed upwards (bucknose). If the bony septum is made smaller through rarification and ulceration, or through imperfect development, there results the deformity spoken of as saddle nose, characterized by a depression of the ridge of the nose. Perfora-

tions of both cartilaginous and bony portions of the septum occur in early hereditary syphilis. A certain number of these children are born with deformities of the nose, frequently with abnormally small, or abnormally flat noses. That which characterizes these noses is the fact that the ridge seems peculiarly broad and deeply sunken between the orbits and that the two nasal passages meet under the ridge of the nose at a very obtuse angle. The cause of this congenital nasal deformity lies in an imperfect fœtal development of the cartilaginous portion of the septum, analogous to the conditions in myxœdema and mongolian idiocy.

The *skin lesions* in hereditary syphilis are very characteristic. Certain forms of these appear only in the congenital, never in the acquired disease. These are syphilitic pemphigus and a diffuse infiltration of the skin.

Fig. 117.

Macular syphilides of the skin of the face with a high degree of diffuse infiltration of the borders of the lips in a child five weeks old.

One must distinguish in early hereditary syphilis of infants between diffuse and circumscribed skin lesions. While the latter, on the whole, correspond to certain changes in the skin found in acquired syphilis, the former give to the child a characteristic appearance which manifests itself primarily in the consistency of the skin of the face. I have called this change diffuse, superficial, syphilide, or diffuse hereditary-syphilitic skin infiltration. Soon after the appearance of the nasal symptoms the skin of the face assumes a peculiar, pale, yellow tint, and is somewhat glossy, symptoms that depend not so much upon insufficient blood supply, as upon a mild infiltration of the papillary portion of the skin and upon increased tension in the rete of Malpighi.

The color resembles at first a pale café au lait, after a longer period of time when more pigmentation has taken place, the color of the finger of a cigarette smoker. These changes are especially marked on the cheeks and on the chin, but also appear like spectacle rims on the orbital borders, or like the expanded wings of a butterfly about the root of the nose, or like a gotee on the under lip.

A diffuse infiltration of the borders of the lips is very characteristic. This produces a peculiar stiffness, a brownish red color, and a striking glossiness (Fig. 117). Soon radial fissures and rhagades appear

in the infiltrated skin areas in those places where muscular action keeps the skin in motion, as about the mouth and nostrils, and on the eyelids. Similar infiltrations affect the hairy scalp leading to loss of hair, and also with great partiality, the skin of the flexor surfaces of the lower half of the body and that of the genito-anal region.

External irritants exert an undeniable influence upon the production of this form of syphilis. This accounts for the predilection for the lower half of the body, which is constantly exposed to the irritating effect of feces and urine. Not rarely one sees in congenitally syphilitic infants during the eruptive stage the conversion of an intertriginous skin affection into a diffuse superficial syphilide, with a change from a light red, oozing skin to one that is brownish and has a peculiar stiffness, dryness, and glossiness. Frequently the skin infiltration is localized on the flexor surfaces of the lower extremities like the leather portion of a pair of riding breeches.

Independently of external macerating influences, the skin of the soles of the feet and of the palms of the hands is always involved at the very first in a diffuse manner, on account of the early and very abundant development of sweat glands in those regions. The skin becomes hard, smooth, and free from wrinkles and glossy as if varnished or painted with water glass, with a color that at first is reddish yellow later brownish, or salmon colored. Very frequently diffuse involvement of the skin of the soles, palms and face, is a forerunner of the appearance of regular, circumscribed exanthemata, frequently, however, it forms the only cutaneous lesion.

Diffuse hereditary-syphilitic skin infiltration may be divided into three forms, or stages, between which transitional forms exist.

1. Diffuse smooth infiltration, or erythematosa simplex. This is frequent on the soles and palms, but also on the chin, on the glabella, on the preauricular hairy portions and about the neck. The color of the smooth scaleless skin that is involved may show all kinds of tints from a light cherry red to the darkest blue red.

2. Diffuse, desquamative, or lamellar infiltration. In this the horny layers of the skin are loosened and separated in large lamellæ, or masses, while the texture of the skin appears sclerosed and very much thickened.

3. Eroded infiltration. This term applies to all ulcerated, oozing, moist, and impetiginous forms.

This diffuse specific skin infiltration can arise under many different conditions: (1) by confluence of a number of disc-like areas the size of a penny to that of a dollar, of pale rose color, not raised above the general surface of the skin; (2) on top of a diffuse uniform erythema; (3) by the rapid confluence of very rapidly arising, small, pale red, closely packed, individual efflorescences; (4) by the confluence of real lenticular papules.

This diffuse hereditary-syphilitic lesion is most frequently found during the first three months of life and, according to our investigations, is never present at birth. It is a very frequent, but by no means constant skin affection of hereditary syphilis that ushers in the period of cutaneous manifestations, but can also reappear at any time during the first year as a recurrence.

A special form of this diffuse skin infiltration in hereditary syphilis is found in specific *paronychia*, which is accompanied by trophic disturbances of the nails (see Plate 26). Two forms are distinguishable: paronychia sicca, and paronychia ulcerosa. The skin adjacent to the bases of the nails of both fingers and toes appears brownish-red, thickened and glossy, and covered with scales, or with crusts. As soon as this specific involvement of the matrix of the nail has persisted for some

Fig. 118. Fig. 118*a*.

Fig. 118.—Diffuse crusty syphilide of the face. Myotonia spastica.
Fig. 118*a*.—Syphilitic pemphigus of the newborn on the soles of the feet in a child seven days old. The skin infiltrated in toto. Pemphigus blebs broken.

time, it is noticed that the nail is divided by a whitish transverse furrow into two parts which seem separate from one another and have very different characteristics. The proximal portion is thinner and marked by longitudinal furrows while the distal portion appears normal, "or at least a somewhat increased brittleness." Very frequently the nails are completely softened or disintegrated.

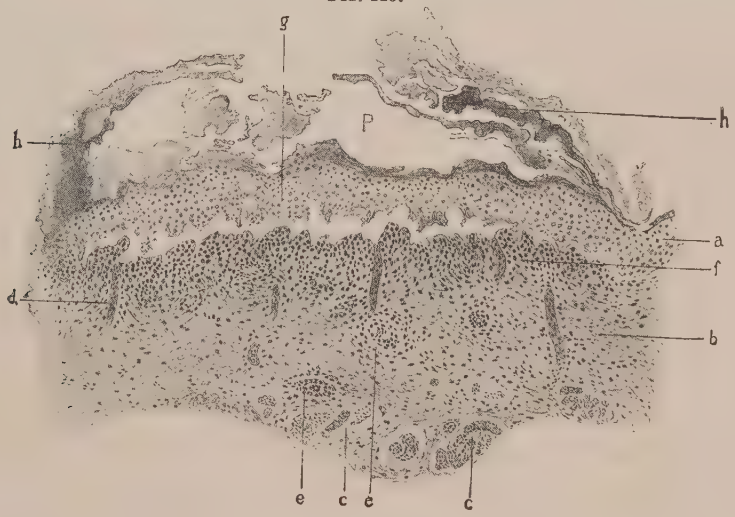
This diffuse syphilide of infancy has a special predilection for the hairy scalp. Whenever a hairy portion of the body is involved this leads at first to a marked increase in desquamation and in sebaceous secretion. Masses of sebum are rapidly formed—much more rapidly than in a simple nonspecific seborrhœa.

The scalp secretion always becomes thicker and tougher, it rapidly dries up with the scales into a hard crusty mass that covers the head completely like a hood. These masses do not, however, as a rule show the straw yellow color of the crusts of simple seborrhœa, but rather are

light brown, with a base of infiltrated, copper-colored skin, not one that is bright red, swollen and oozing. At the same time the scales are always less firmly united to the skin than in eczema with crusts, and can usually be picked off without causing bleeding.

It is also very significant that the affection almost never moistens the scalp, as opposed to the condition in eczema. Under these masses of sebum there is usually found in these cases of diffuse syphilide of the scalp, a perfectly intact epidermis, while in seborrhœal infantile eczema of the scalp, when the crusts are lifted, the bared rete Malpighii is exposed, or if still more intensely inflamed, the bleeding papillary layer.

Fig. 119.



Vertical section of a syphilitic pemphigus bleb on a diffusely infiltrated plantar skin area. (*a*) rete Malpighii, infiltrated with round cells (*g*); (*h*) horny layer torn and lifted up in a number of layers; (*b*) corium with proliferated connective tissue cells; (*c*) sweat glands; (*d*) gland tubules ending in the papillary layer without connection with the epidermis; (*e*) a section of blood vessel with perivascular granulations; (*f*) greatly infiltrated and swollen papillary portion; between *a* and *f* is a close space resulting from the separation of the rete Malpighii from the papillary layer; (*P*) pemphigus bleb. (Slight magnification.)

This same process manifests itself in a very similar manner in the region of the eye-brows. In many cases an early diffuse involvement of all the hairy regions leads to complete alopecia. The characteristic absence of hair on the scalp and on the eye-brows and eye-lashes in older infants afflicted with hereditary syphilis is explained in this same way.

Occasionally there is a facial eczema implanted upon the diffusely infiltrated skin of hereditary syphilis (Fig. 118). On the borders of the eyelids, the nostrils, and the lips, the infiltrated skin easily cracks and so leads to crust formation. Apart from the rhagades the whole skin of the face may be covered with reddish-brown or brownish-yellow crusts. In severe cases a rupiaform syphilide results.

The Circumscribed Exanthemata of Early Hereditary Syphilis.—These appear either upon a diffuse skin infiltration or upon a previously unaltered skin.

Pemphigus Syphiliticus Neonatorum.—In the majority of cases this is present at birth, occasionally it appears during the first week, rarely during the second to the fourth week. If present at birth, or occurring during the first few days, it has an ominous significance, less so if it occurs later. Essentially there is no difference between these two forms of pemphigus, which would be more properly designated by the terms papulo-bullous, or papulo-pustular, syphilide. In pemphigus of the newborn we have an eruption composed of vesicles or blebs, varying in size from that of a pea to that of a penny, filled with purulent or bloody

Fig. 120.

Fig. 121.

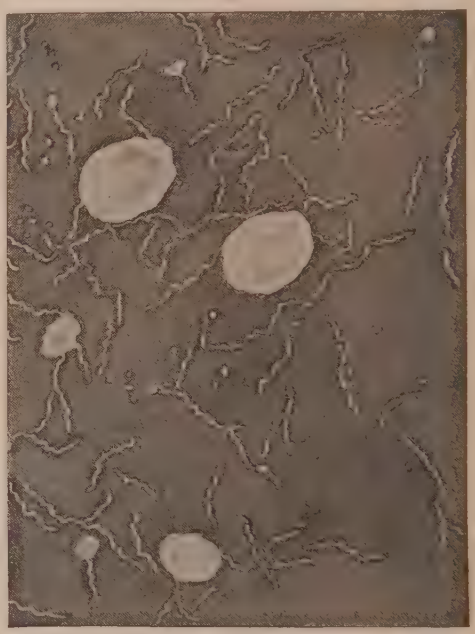


Fig. 120.—Isolated papules on the forehead. Hydrocephalus in miniature. Saddle nose.
Fig. 121.—Spirochæte pallida in secretion of papule.

fluid, and located on disc shaped brownish red spots. The blebs are surrounded by an infiltrated border. They always appear first on the soles of the feet and on the palms of the hands, but can later invade other regions of the body, not, however, without being preceded by an infiltration of the skin (Figs. 118*a* and 119; and Plate 28). As a result of the confluence of several blebs and the destruction of their roofs, ulceration takes place, and in rare cases circumscribed gangrene of the skin may supervene. Streptococci and staphylococci are found in great numbers in the secretion within the blebs. Schaudinn's spirochæte pallida, too, has recently been found repeatedly.

The form of eruption that I have designated as *late pemphigus* has the same localization as the early form which is present at birth, or

PLATE 28.

II. Maculo-papular syphilide in hereditary syphilis.

I. Pemphigus syphilitica.

within a few days after birth, but appears more frequently superimposed on an area of diffuse skin infiltration (see Plate 29).

Histologically there is in both forms a uniform inflammatory cell proliferation of the papillary portion, following the blood vessels. There is a striking broadening and a serous imbibition, on the part of the papillæ and a separating from them of the rete mucosum, so that within the area covered by the bleb there is a complete denudation of the papillæ of their epidermal covering (see Fig. 119). At the same time there occurs splitting of the horny layer itself.

The remaining early exanthemata of hereditary syphilis differ but little from those of acquired syphilis. The following forms of eruption may be distinguished:

1. *Maculopapular Syphilide.*—(Figs. 117, 120, 122 and Plate 28). This occurs as a rule after a period of incubation lasting several weeks, and consists of more or less numerous disc-shaped spots, slightly raised above the general skin level, varying in color from an early rose red, to a later brownish, or ham color, or after persisting for some time, to an ochre yellow. The locations of predilection are the lower extremities, the flexor surfaces of the upper extremities, the neck, chin and face. Palms and soles, too, are frequently affected. The papules may be absorbed from the centre leaving pigmented spots, or they may undergo desquamation, or in the presence of mechanical irritation they may grow extensively in all directions, and form the so-called condylomata lata. The latter never appear as the first eruption of congenital syphilis, but are always an expression of a relapse. They occur usually in places where two opposing skin surfaces rub together as in the circumanal and genitocrural regions, in the interdigital folds and about the navel. They are easily eroded and then show a lardy yellow, or diphtheroid, surface. When the secretion ceases and the condylomata dry up, the color becomes lighter, the centres become depressed and the growths are covered with a layer as if they had been painted with collodion.

In early congenital syphilis the roseola of the acquired type is never found. Likewise the trunk is usually wholly free from eruption in the congenital variety.

The papular eruption may be the first exanthem in congenital syphilis or may represent a relapse of the disease. In the latter case it has been preceded either by diffuse skin affections, or simply by visceral and osseous manifestations.

Occasionally vesicles and pustules arise from broad papules by elevation of the epidermis.

The favorite location of maculopapular eruptions is the forehead and the hairy scalp, usually after the diffuse skin infiltration has preceded it. A dense crown of papules is frequently formed on the forehead in relapses.

Most of the papules disappear ultimately by simple absorption, those that are larger and more elevated after a preceding desquamation, the oozing forms after a preceding crust formation.

When crust formation has taken place extensively on the face and on the hairy scalp, there is an appearance that greatly resembles the stages of crust formation in impetiginous eczema. But the brownish yellow borders of the infiltrate with their glued appearance, as well as the crust-free infiltrated skin areas with their almost metallic lustre, the peculiar stiff, reactionless character of the whole inflammatory picture, and the absence of serous discharge between the scabs point to the fact that back of this crust formation there is not an eczema, but a syphilitic infiltration.

2. *Papulopustular Syphilide.*—This form of eruption has a relatively short incubation period. Pustules with thin purulent contents,

Fig. 122.

Maculopapular syphilide of the skin of the face and extremities. Trunk free. Nose sunken in. Rhagadic ulcers on the infiltrated borders of the lips. Myotonia perstans.

not unlike the pustules of smallpox, appear on deep red flattened papules about the size of a lentil. Usually they appear only as scattered lesions. Through drying of the contents of the pustule cupshaped crusts frequently are formed (rupiaform syphilide). Frequently deeper ulceration takes place with the formation of crusts that resemble oyster shells (ecthyma syphiliticus). These forms belong to the severe manifestations of infantile syphilis and give an unfavorable prognosis. One must not confuse with these pustular syphilides secondary septic, or pyæmic skin lesions in children that have hereditary syphilis.

3. *Ulcerative Syphilide.*—In locations that are naturally exposed to maceration and are not kept clean, ulcers are formed through the destruction of papules. These are characterized by a peculiar basin-like, sunken surface, by a dry, shining coat, and by its infiltration wall and absence of reaction. The site of predilection is the genito-anal region. But in other regions too papules may become eroded and ulcerated when exposed to mechanical and chemical irritation. Furthermore, all forms of vesicular and pustular syphilides may lead to

ulceration. These ulcers are all distinguished from nonsyphilitic ulcers by the absence of inflammatory reaction, by the small amount of pain, by the presence of peculiar, dry, firmly adherent crusts and by their central depression. Probably all pustular and ulcerative syphilides depend upon a double infection, *i.e.*, with the specific germ of syphilis and with pyogenic bacteria.

4. *Small Papular Syphilide.*—This is extremely rare in infants and according to my observation occurs only as a manifestation of a relapse in hereditary syphilis during the second half of the first year. It greatly resembles tubercle of the skin (tuberculides), but is distinguished by the brownish color, the peculiar glossiness, and the hardness of the individual papule. I have seen it on the nape of the neck, the back, the forehead, and on the extremities, partly scattered, partly arranged in groups. At most the papules are but few in number. Exceptionally I have seen this form of eruption arise as late as the second or third year. This syphilide is very intractable from a therapeutic standpoint.

FIG. 123.

Papulopustular syphilide (late pemphigus). Child of four weeks. Lesions chiefly on the extremities, more especially the lower ones. Among simple papules others that are surmounted with vesicles. In addition osteochondritis of the left humerus and ulna with swelling of affected joints and flaccid paralysis.

Lesion of the Mucous Membranes.—Apart from nasal affections that have already been discussed, involvement of the mucous membranes in hereditary syphilis during infancy is a rare occurrence. Diffuse infiltration and papule formation, it is true, favor, as already indicated, the regions about the openings into the body, thus bordering on the adjacent mucous membranes without however invading the latter. Occasionally a stubborn hoarseness amounting even to aphonia indicates an involvement of the laryngeal mucous membranes, but only exceptionally during or soon after the first eruption. Usually this is one symptom among others of a relapse in which, as a result of œdema of the glottis and perichondritis, severe attacks of suffocation can occur that may even necessitate tracheotomy.

In spite of the intimate connections between the nasal mucous

membrane and that of the middle ear, and in spite of the rather frequent attacks of middle ear disease in infancy, discharge from the ear is a rare affection in early hereditary syphilis.

A typical involvement of a mucous membrane is to be found in Mracek's *syphilis annularis intestini* localized in Peyer's patches. This, together with diffuse thickenings of the gastro-intestinal mucous membrane that are a result of inflammatory cell infiltration areas accompanied by partial disappearance of the glandular elements, is perhaps the cause of intestinal disturbances in infants with congenital syphilis, although other factors doubtless play a part.

Fig. 124.

Sagittal section of the knee-joint of a macerated fœtus with hereditary syphilis in the last lunar month of pregnancy. Wegner's osteochondritis, second stage. *A*.—Broadened irregular zone of calcification with serrated border; long projections into the hyaline cartilage. *B*.—Very wide medullary space with granulation tissue. *C*.—Hyperæmic layer of spongiosa, adjacent to the medullary space.

In children that are born healthy the *first evidence of syphilis* is nearly always to be found in symptoms of disturbed general health, with nervous unrest, increased tension in the fontanelle, rise of temperature, and deficient gain in weight. The appearance of diffuse skin infiltration and papular eruption is accompanied in my experience by only slight rise of temperature, while the eruption of pustular syphilides always brings out a temperature up to 39° C. (102° F.) lasting for a number of days, and frequently lasting many days longer than the eruption itself, probably due to a mixed infection.

Changes in the blood picture are always found soon after the eruption begins, but very frequently also before that time. They consist in a diminution in the amount of hæmoglobin and in the number of erythrocytes together with the appearance of many nucleated red blood corpuscles and an increase in the number of white blood cells, especially the myelocytes and eosinophiles.

From a diagnostic standpoint it must be remembered that lesions of the skin and of the mucous membranes may be very insignificant and that the diagnosis of early hereditary syphilis must not depend upon the presence or absence of skin lesions.

Bone Lesions in Early Hereditary Syphilis.—The osseous system is involved at least as frequently as the skin in hereditary syphilis. Involvement of the bones that are preformed in cartilage nearly always begins in intra-uterine life, while that of the bones that form in membranes usually occurs after birth. In fact Wegner's osteochondritis which occurs at the epiphyseal borders of the hollow bones is a fœtal manifestation, while the hyperostoses of the cranial bones usually do not arise until after birth.

PLATE 30.

II

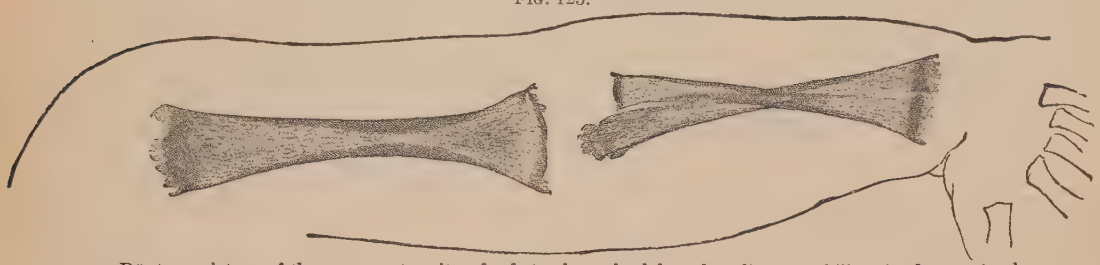
I

I. Syphilis hereditaria tarda of the left ulna in a 10-year-old boy. Spindle-form enlargement at middle of ulna due to ossification of a periosteal proliferation.

II. Syphilis hereditaria tarda. Ten-year-old girl.

The explanation for the innate relationship between the poison of congenital syphilis and the fœtal osseous system is to be found in the

Fig. 125.



Röntgen picture of the upper extremity of a fœtus born dead from hereditary syphilis. At the proximal end of the humerus and at the lower ends of the diaphyses of the forearm marked broadening of the zone of calcification with pointed projections toward the epiphyses. At the distal end of the upper arm behind the rather strongly rarified zone of calcification well marked lightening of the diaphyseal shadow. (Natural size.)

powerful and peculiar method of growth of the skeleton, which has this peculiarily, that it grows, not uniformly, but by apposition either through metaplasia of cartilage or through increase from the periosteum. Those portions of the bony system in which growth is most active are the ones that most attract the poison of syphilis circulating in the fœtal organism, and so there arises in fœtuses and young infants that affinity for the epiphyseal borders of the long hollow bones and for the tuberosities of the cranial bones. In this so-called osteochondritis heredosyphilitica of Wegner the most prominent changes that are found are disturbances in the metaplasia of the cartilaginous ground substance about the intrachondral medullary spaces, abnormal proliferations of cartilage cells, necrotic processes within the cartilage, intrachondral cleft formation, and pathological calcification.

Fig. 126.

Röntgen picture of the lower extremity of a syphilitic newborn child. Broadening of the zone of calcification with a ragged edge toward the epiphyseal cartilage. (Natural size.)

In the zone of the subchondral medullary space formation there occur at first hyperæmic inflammatory processes with simultaneous transformation of the marrow of the spongy portion into granulation

tissue and the failure of osteoblast formation. Frequently before this time changes in the consistency of the marrow have appeared at the diaphyseal ends with retrogression of vascularization. The marrow at the cartilaginous borders often becomes transformed into fibrous connective tissue.

The disturbances of periosteal and perichondral ossification consist at first of subperiosteal envelopment of granulation tissue, from which results a melting, as it were, of the compact bony substances. Through calcification of this granulation tissue there arises abnormal hyperostosis, often even the formation of many layers about the primary bone which is embedded in the new shell of bone, like the end of a cigarette in its holder. Besides this ossifying periostitis there is also a chondrifying periostitis in the region of the epiphyseal borders, if within these there is taking place, or has taken place, a break in continuity. Under these conditions there can occur, just as in real fractures, the formation of genuine callus, at first cartilaginous, later bony.

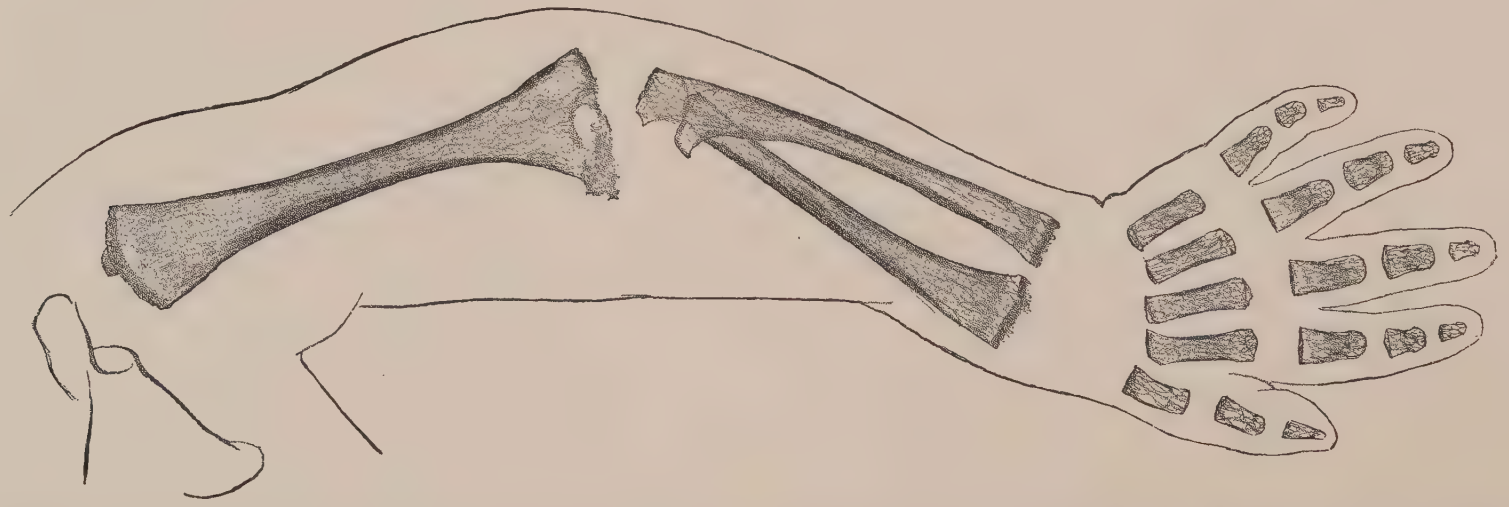
According to Wegner (1870) three stages of osteochondritis can be distinguished. In the first stage the zone of calcification of the cartilage is broadened and irregular, distinguished from the bluish shimmering cartilage and from the strongly hyperæmic spongiosa by its greater density and lighter color. The second stage is characterized by the establishment of a broad mortar-like layer belonging to the provisional zone of calcification between the epiphyseal cartilage and the diaphysis. In the third stage there follows in connection with the hyaline cartilage toward the diaphyses a wholly irregularly defined layer several millimetres wide of a grayish yellow mortar-like mass which is very compact (broadened, irregular calcification of cartilage). Next to this is a grayish yellow or grayish red layer of varying width and of light density, that gradually disappears as the spongiosa is approached. On account of this mass of slight resistance the natural connection between epiphysis and diaphysis is disturbed, frequently to such an extent that the shaft of the bone remains attached to the epiphysis only through the thickened periosteum.

The beginning stages of osteochondritis are usually not recognizable macroscopically, but can be demonstrated microscopically.

With reference to the anatomical conditions in separation of the epiphyses in hereditary syphilis, one must remember that this is essentially a fracture which takes place either in the subchondral granulation tissue, or, if necrotic processes exist, in the columnar portion of the cartilage. Lessening of density, trauma, and muscular action, are the causal factors. For this reason epiphyseal separation in hereditary syphilis occurs only in the long hollow bones, never in the ribs, or short hollow bones.

The short hollow bones show intrachondral and periosteal pathological processes that are quite similar to those found in the long bones.

FIG. 127.



Semidiagrammatic Röntgen picture of a congenitally syphilitic child three months old with paralysis of the arm. Widening and jagged end of the zone of calcification at the distal epiphysis of the forearm; toward the diaphysis very light transverse shadow, corresponding to the high degree of rarification of the bony trabecular system in the zone of medullary space formation, besides periosteal deposits and swelling of the ends of the bones. In the median portion of the distal epiphysis of the humerus, separation of the latter with callus formation, appearing as an irregular shadow occupying a portion of the end of the bone; behind this a clear area filled only with granulation tissue without bone. The zone of calcification at the upper end of the humerus is decidedly widened.

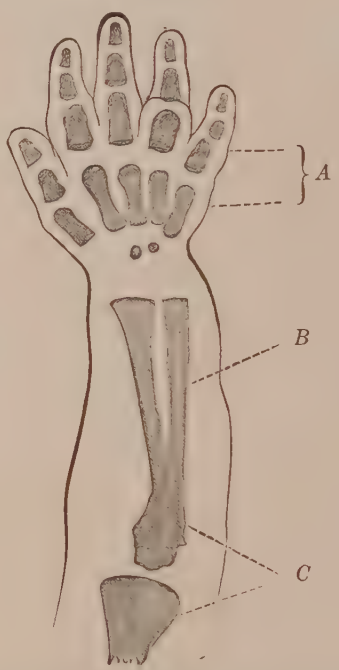
There are disturbances in the endochondral ossification and rarifying diaphyseal processes, and also characteristic periosteal affections. Separation of the epiphyses and involvement of the small joints are never found.

Joint affections are very rare in hereditary syphilis during the first year, but they do occur during the second year, especially in the larger extremities, but only rarely in those connected with the vertebral column. Joint suppuration in syphilitic infants is always the

Fig. 128.

Semidiagrammatic Röntgen picture of the right hand of a three and one-half months old child, with epiphyses of the forearm formerly separated and poorly united. Pathological inflammatory calcification of the epiphyseal cartilage. Also multiple involvement of the short hollow bones.

Fig. 128*a*.



Semidiagrammatic Röntgen picture of the left upper extremity of a child two and one-half months old with general involvement of the whole osseous system and pseudoparalysis of both upper extremities. Phalangitis, endosteal and periosteal disease of the long hollow bones. *A*.—Rarefying osteitis of the short bones with swelling and faint shadow. *B*.—Diffuse periosteal osteophyte of the bone of the forearm. *C*.—Swelling and rarefaction at the diaphyseal ends.

result of mixed infection. The confounding of gonorrhœal and pyæmic joint inflammations with osteochondritis of congenitally syphilitic origin has doubtless occurred many times, especially since the extremities are found in positions that suggest paralysis in all of these conditions.

Radioscopy is of great importance in hereditary syphilitic lesions of the osseous system.

Syphilitic osteochondritis is demonstrable in X-ray pictures of older fœtuses and widening of the zone of calcification with its irregular jagged border can regularly be made out in dead specific fœtuses (Figs.

Fig. 129.

Radiograph of upper extremities of a two-month-old congenital syphilitic infant with Parrot's pseudo-paralysis.

The soft parts about the elbow-joint are distended and the muscles inflamed. The ends of the diaphyses are mushroom-shaped on account of periosteal callus formation.

Fig. 129*a*.

Radiograph of lower extremities in the same case.

125 and 126). In living infants too, with syphilitic infection, if kept absolutely quiet, the presence of general affections of the osseous system of osteochondral or periosteal nature in the long and short hollow bones, which have not caused clinical symptoms can frequently be discovered. The so-called pseudoparalysis heredosyphilitica (see later) has always shown, in those cases I have examined with the X-ray, recognizable changes in the osseous system, which have consisted in lessening of the diaphyseal shadow, or in periosteal hyperostosis, or in swelling of the bone (Figs. 127 and 128). In genuine separation of the epiphysis there is shown a periostealinflammatory lime deposit at the diaphyseal border which extends over to the epiphysis and may produce very irregular shadow effects of the latter.

FIG. 130.

Longitudinal section through the tibialis posticus muscle below the upper tibial epiphysis in a congenitally syphilitic child of 2 months, together with the periosteum and periosteal inflammatory proliferation. *O.*—Calcified osteoid originating in the inflamed periosteum. *K.K.*—Cartilage callus, chondroid proliferation within newly formed bone resulting from inflamed periosteum. *Pe.*—Swollen and œdematous fibrous layer of the periosteum with spaces between the bundles of elastic fibres. *Ih.*—Focus of infiltration of round cells extending from the inflamed periosteum toward the muscle; the sarcolemma of the latter is much disintegrated. *Bg.*—Blood vessels with perivascular inflammation and proliferation of intima. *Me.*—Inflamed and disintegrated bundles of muscle fibres, cut longitudinally and diagonally, with infiltrated perimysium (*Pm*). *Mr.*—Remnant of muscle tissue little changed. *N.*—Cross section of normal new fibre.

Affections of the Short Hollow Bones.—The hereditary syphilitic lesions of the bones of the fingers and toes in infants were only rarely described before my own investigations were made. Specific involvement of the phalanges, which occurs much more frequently in infancy in the fingers than in the toes, affects only the bones of the phalanges, never the soft parts and always begins in the proximal phalanges. The latter are also more intensely affected in the further course of the disease than are the distal phalanges.

The X-ray picture of the diseased phalanges shows three degrees of shadow: a moderate lessening of depth of shadow of the epiphyseal borders, a still greater one of the diaphyses and a dark faint shadow; but a sharply defined marginal shadow corresponds to the compact portion of the bones. At the same time the bone seems abnormally swollen both as to width and length (Fig. 128*a*). All of this points undeniably to the fact that in phalangitis there is, from a pathological standpoint, a diffuse rarefying osteitis of the phalangeal bones, that occurs much more frequently than is usually thought to be the case from mere clinical examination.

From a clinical and diagnostic standpoint the following facts are important: the predominating involvement of the basal phalanx, the absence of suppuration or of external perforation, the tendency to spontaneous restitution and the subacute course of the disease. This painless swelling, involving first the proximal phalanx, and always the bone only, gives to the finger the form of a bottle: with simultaneous involvement of the distal phalanges it takes the form of a tenpin. The finger always appears broader as well as longer. The soft parts do not take part in the disease but the skin, on account of stretching, may become glossy, tense and peculiarly rosy—sometimes it may even appear thinned. The index finger is most frequently affected. These lesions tend to multiplicity but not to symmetry. A further characteristic lies in the complete absence of involvement of the joints adjacent to the diseased phalanges. This affection belongs to the early manifestations of hereditary syphilis, and is insidious in its development, without causing functional disturbances.

Hereditary syphilitic disease of the fingers after the first year of life no longer shows the above characteristic and unvarying type; caries may now appear, as well as involvement of the joints and soft parts.

From a differential diagnostic standpoint *spina ventosa scrofulosa* needs consideration, especially if only the basal phalanx of one finger is affected. Here there must be considered the history, the age of the child, the possible presence of other symptoms of syphilis, especially the characteristic nasal affection, then various anatomical factors such as absence of suppuration, caries, and necrosis, non-involvement of the skin as well as the shape of the diseased finger, knob-shaped in the scrofulous, olive shaped or conical in the specific disease. Appearance in earliest infancy of the involvement of the phalanges, or of the basal phalanges of all fingers, or of several fingers, would always speak for syphilis.

From a clinical standpoint, in this early period, only those bone changes are recognizable in which the periosteum is also involved. The finer changes at the cartilaginous borders of the bones cannot be made out by palpation, but can be demonstrated radioscopically.

Very frequently a radioscopic examination in syphilitic infants will show that the whole osseous system has been changed in toto while only a few bones will show any pathological changes clinically. (See Figs. 127, 128 and 128*a*.)

The most prominent manifestations are swelling in the region of the epiphyses of the long hollow bones, and motor disturbances.

These swellings that form a spindle-shaped extension from the diaphysis to the epiphysis affect especially the periosteum and the surrounding soft parts. The periosteum appears thickened, with a jelly-like infiltration and is permeated in different layers by ossifying or chondrifying proliferations. Quite frequently all of the tendon inser-

Fig. 131.

Pseudoparalysis of the right upper extremity in a syphilitic child with eruption. Swelling of the region of the elbow-joint. Spasm of the hand. Myotonia of the extremities that are free from paralysis.

tions and all of the muscle bellies surrounding the diaphyses are fused together into one uniform jelly-like mass.

Such swellings may be found in the region of one or more joints. The elbow-joint is most frequently involved. The swollen portion is nearly always decidedly tender.

Two kinds of motor disturbances must be distinguished, the paralytic and the spastic. The latter can be grouped together as the syphilitic myotonia of infancy. Myotonia may cause inability to move an extremity, but is nevertheless always a spastic condition as opposed to the so-called Parrot's pseudoparalysis, which represents a flaccid paralysis of the arm with more or less pain, and resulting from syphilitic inflammatory involvement of the bone and muscles. It is an important fact that in syphilitic bone disease of the lower extremities contractures result, while in the upper extremities we have instead a flaccid paralysis, a phenomenon that is dependent upon the different relations of the

musculature to the large joints in the upper and lower extremities. The occurrence of muscle involvement in the extremities in early hereditary syphilis is of great importance (Fig. 130).

One always finds specific vascular changes in the affected muscles in which interstitial as well as parenchymatous and degenerative changes are demonstrable. The nerve-fibres, on the other hand, have always remained unaffected in those cases that I have examined. It is evident that such myopathies can lead to paralytic manifestations. As a rule myostitis starts from an inflamed periosteum, but is may arise independently. A warning must be given however against the too rapid diagnosis of gumma in the case of a nodule in the sternocleidomastoid muscle of the newborn child. Even in syphilitic children this is always a traumatic hæmatoma.

The clinical manifestations in the bone system in early hereditary syphilis consist of swelling of the bones and restricted motion, which are often associated with swelling of the soft parts, separation of the epiphyses, and crepitation.

The possibility of the occurrence of paralysis of central origin in early hereditary syphilis cannot be positively denied. It must be said, however, that the findings that we have up to the present time (Schlichter, Zappert, von Peters, Scherer) do not suffice for the establishment of a spinal basis for these congenitally syphilitic motor anomalies in infancy. In most cases of supposed spinal etiology we have either a simple birth palsy, with or without syphilis, or a continuous spasm of toxic origin, which may occur as well in syphilitic as in other children. The clinical picture of this form of paralysis may be a very variable one. Almost without exception flaccid paralyses are located in the upper extremities and resemble those resulting from peripheral plexus lesions in which there is not necessarily always much pain in the extremity. There are paralytic manifestations in hereditary syphilis in which the whole upper extremity appears paralyzed, even dangling; then again others in which the type of an upper arm paralysis is most prominent, and finally those in which there is rather a forearm type of paralysis.

According to my investigations these paralytic manifestations are always the result of muscle involvement alone, which probably in most cases takes its origin in inflammatory periosteal affections. Since the muscle disease, in the absence of severe periosteal involvement, is not by any means always painful, it is easily seen why severe pain is as frequently absent in pseudoparalysis. The Klumpke–Déjérine type of paralysis with involvement of the oculopupillary fibres is not a form of specific motor disturbance in infancy but is rather to be attributed to obstetrical plexus paralysis, if found in hereditary syphilitic newborn and older infants.

These paralytic appearances may manifest themselves suddenly,

Fig. 2.

Fig. 1.

Fig 3.

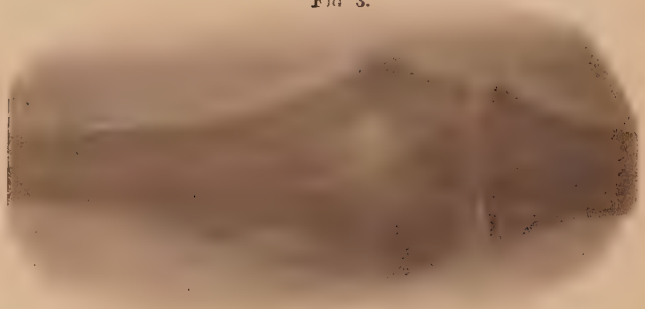


Fig. 1.—Diffuse hyperplastic periostitis of the bones of the upper extremities in a six-months-old syphilitic infant. Ossifying chondritis of the epiphyses, which present an angular fracture opposite the axis of the diaphysis where spontaneous healing has taken place. A permanent flexion contracture of the elbow-joint resulted from the fracture of the epiphyses.

Fig. 2.—Diffuse periostitis of the lower leg in the same child. Enlargement of the knee and calcification of the distal epiphysis of the femur.

Fig. 3.—Recent node on the external condyle of the right femur in an eleven-year-old child with congenital syphilis.

Fig. 4.—Diffuse periosteal enlargement at the distal end of the right humerus in a nine-year-old child with congenital syphilis.

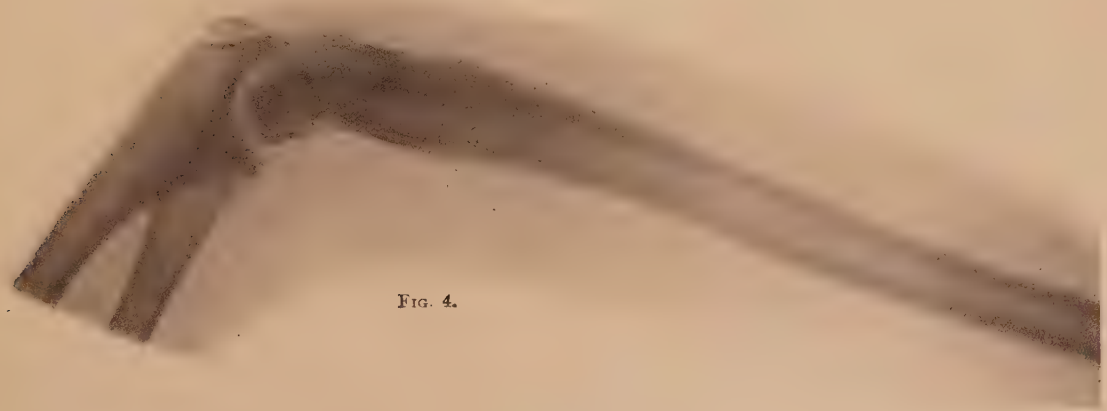


Fig. 4.

in one night, or gradually. In the upper extremities hereditary-syphilitic bone diseases always give the picture of flaccid paralysis, in the lower extremities that of the spastic type.

The skull in hereditary infantile syphilis may present four types of changes:

1. Simple rachitic changes which manifest themselves in softening of the bone in the squamous portions, and along the sutures, and are not distinguishable from ordinary rachitic changes, especially from craniotabes. These frequently occur during the first few months of life.

2. Abnormal protuberance of the frontal and parietal eminences with striking hardness of the cranial bones and of the sutures, due to an early periosteal hyperostosis of these bones. This occurs during the first few months of life but is not so frequent in early infancy as the preceding type.

3. Periosteal swelling and rarefaction of the bone in isolated or extensive areas, due to a specific inflammatory involvement of the cranial bones. This is the rarest syphilitic lesion of the skull bones during the earliest period of life, and is characterized by areas of wasting (caries sicca) surrounded by walls of bone.

4. Hydrocephalus. In earliest childhood this is, in a good many cases, caused by hereditary syphilis. The latter can produce inflammatory changes in the meninges and plexuses, and even lead to disease of the intracranial vessels, simulating tuberculous meningitis. Frequently, a specific diffuse periostitis of the inner surface of the cranial bones is the starting point for a meningitis. Specific hydrocephalus of infancy has a superficial resemblance to rachitic pseudohydrocephalus, but can be distinguished from it. In a large number of cases syphilitic hydrocephalus is curable by the use of iodides and mercury.

A close relationship exists between hereditary syphilis and rachitis.

Among children afflicted with hereditary syphilis, rachitis is somewhat more frequent than among those that are free from this disease. Rickets begins earlier in syphilitic children, has a more rapid course, but only rarely leads to a high degree of bone deformity.

The circumference of the skull in infants with hereditary syphilis is greater during the whole of the first year than in those that are normal because of the greater bone formation at the centres of growth of the squamous bones due to specific excitation. During the first half year it exceeds that of rachitic children, and only during the second half year of life are the skulls of rachitic children larger than those of children with hereditary syphilis. As a consequence there is a peculiar shape to the upper surface of the cranium, characterized by the prominence of the frontal and parietal eminences, while between the latter there is a more or less well marked furrow. This cranial anomaly, called caput natiforme by Parrot, can only then, with certainty, be laid to heredi-

tary syphilis, when it is well developed during the first few months of life and is associated with an abnormal hardness of the skull bones and with a relatively small fontanelle; the same shape occurs also in the heads of rachitic children who are free from syphilis, during the second and third year of life.

If the caput natiforme is associated with microcephalus without well marked rachitic changes in the thorax and extremities, this speaks absolutely for hereditary syphilis. On the other hand, the combination of a high degree of rachitic deformity of the extremities and this form of head almost positively excludes a syphilitic origin, because we know from experience that syphilitic children only exceptionally become severely rachitic.

Liver Affections.—Hereditary syphilitic disease of the liver in infancy differs but little anatomically from the changes previously discussed that occur in the fœtus and the newborn child, except that syphilomatous nodules, considerable induration and constriction of large portions of parenchyma by contracted interstitial cell infiltration, together with diffuse cell proliferation, are all met more frequently.

The manifestations in the liver may be either a fresh diffuse interstitial process which causes the organ to increase in size while remaining soft, or an indurative inflammation with connective tissue proliferation and palpable increase in inconsistency. A termination in cirrhotic contraction is not found in infancy. Likewise I could never demonstrate any considerable degree of ascites in hereditary syphilis of the liver in infancy, while in later childhood icterus as well as ascites are common in this condition.

The most important clinical symptom is increase in size. I found this in 31 per cent. of hereditary-syphilitic infants, always in conjunction with a varying degree of enlargement of the spleen. It must be admitted that enlargement of the liver can arise also from stasis, fatty infiltration, etc., and that the liver can normally extend more than 1 cm. beyond the costal border in the parasternal and mammillary lines. A comparison however of the frequency of occurrence in nonsyphilitic and syphilitic children showed that in scarcely 3 per cent. of children under six months old in whom there was no suspicion of syphilis was there present a projection of the liver beyond the costal border in the mammillary line while it was present in 31 per cent. of syphilitic children. This alone would seem sufficient to prove that such enlargement of the liver is due to syphilis even if there is no demonstrable hardening of the organ present.

Besides this simple enlargement of the liver in hereditary-syphilitic infants, which promptly retreats under specific treatment, there is still another clinical form, the *hyperplastic indurative* type, in which the organ in some cases occupies a large part of the abdominal cavity and can be

felt as a hard body, frequently with an uneven surface. Children affected with this form of liver lesion are usually born with it in its fully developed state; they show a distended abdomen with well marked, visible, engorged veins, a hard enlarged spleen, and rarely also icterus. The length of life of infants affected with this form of liver disease is a short one. Whether early hereditary syphilis is capable of producing a hypertrophic biliary cirrhosis has not been decided with certainty. Frequently congenital icterus due to obliteration and agenesis of the gall-passages has been attributed to syphilis, but erroneously, unless there were other manifestations of that disease.

Chiari, Beck and others have described in the newborn a gummatous inflammation of the large bile-passages with termination in contraction, induration and bile stasis; Schüppel has pointed out the occurrence of a contracting peripyophlebitis in syphilitic fœtuses.

It is an important fact that all of these enlargements of the liver accompanied by icterus thought to be due to syphilis were present at birth; while those cases that occur in hereditary-syphilitic infants after birth run their course as a rule without icterus.

Affections of the Kidneys.—It is certain that in infants with hereditary syphilis there is seen during the stage of eruption a clinical picture analogous to that of acute nephritis, which disappears under specific treatment. I, myself, then Bradley, Oedmansson, and Finkelstein have seen cases of that sort. On the other hand albuminuria and casts in congenital syphilis are frequently due to severe, complicating intestinal disturbances, without having any connection with syphilitic kidney involvement, the existience of which however, as previously stated, is undoubted (Hecker, Hochsinger, Schlossmann, Karvonen, Stroebe, Stoerk).

From an anatomical standpoint there are found, besides the diffuse interstitial cell proliferation of the connective tissue about the vessels, parenchymatous changes in the renal epithelium and developmental anomalies in the glomeruli of the cortex.

Clinical manifestations on the part of the circulatory system are rare as a result of hereditary syphilis in infancy, although parenchymatous, fibrous, and focal lesions of the heart muscle and endocardium are observed.

The relations of hereditary syphilis to cardiac and vascular changes will be discussed more fully in the part dealing with diseases of the circulatory apparatus. I will merely mention here that the myocardium of hereditary-syphilitic infants is very frequently occupied by foci of coagulation necrosis which were once erroneously thought to be gummata, and that, according to Winogradow, there are changes in the automatic ganglia of the heart.

Hæmorrhages from the navel in congenitally syphilitic new-

born infants are much more frequently due to changes in the walls of the umbilicial vessels which hinder their contraction, than to septic infection.

True syphilitic endoarteritis is usually not fully developed until the second half of the period of infancy and then involves primarily the cranial vessels, giving rise to foci of encephalomalacia. General involvement of the middle arteries has often been observed (Berghinz).

Children with hereditary syphilis frequently have distended vessels of the skull (Fig. 132) which are not, however, as E. Fournier thinks, due to a parasyphilitic dystrophy of these veins, but are caused by hydrocephalic involvement of the inside of the skull. In the same manner the medusa-like appearance of the veins of the skin of the trunk may be dependent on cirrhotic changes in the liver.

Hereditary syphilis of the lungs occurs occasionally, though rarely, in infants that survive, as a residue from the diseased fœtal condition. As a rule, lung infiltrations of syphilitic infants depend upon secondary infections.

Early hereditary syphilitic involvement of the gastro-intestinal mucous membrane has been mentioned before, but is not recognizable clinically. Exceptionally it may lead to hæmorrhage from the bowel as a result of ulceration of annular infiltrations of the mucosa.

Changes in the Central Nervous System.—These are not rare during the eruptive period of infantile syphilis and manifest themselves clinically by great restlessness and broken sleep. Increased tension in the fontanelles is very frequently demonstrable during this period in connection with these symptoms. Involvement of the brain and its meninges is more frequent than that of the cord. The most frequent lesion to be found in this connection is a *meningitis serosa interna* and *externa* with involvement of the arachnoid and of the chorioid plexus, appearing in the form of an acute, or chronic, hydrocephalus. This very frequently develops during or at the end of the first eruptive period, or occasionally in connection with a relapse. More rarely it is present at birth.

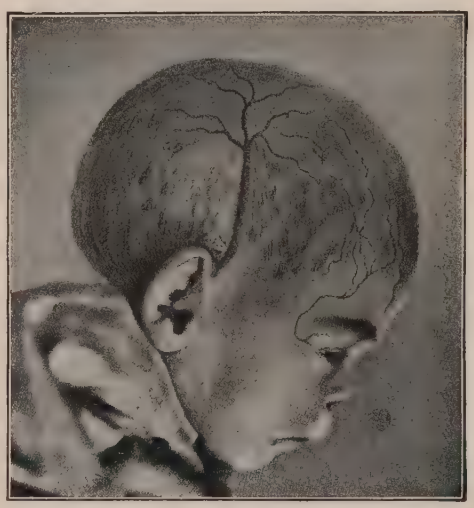
The hydrocephalic head of congenital syphilitic origin does not, as a rule, attain the enormous size of the nonspecific form; but at times, baloon-shaped enlargements occur in that form of syphilitic hydrocephalus which is present at birth (Figs. 132 and 133). In the cases that begin after birth, an early hyperostosis of the cranium prevents enormous enlargement. Here the diagnosis of an increased amount of intracranial fluid, a miniature hydrocephalus, as it were, must be made from the tense and bulging fontanelle, the moderate enlargement of the head, and the characteristic hydrocephalic facies. This syphilitic hydrocephalus of infancy may arise very acutely with the picture of meningitis, or it may occur insidiously without marked functional disturbance of the central nervous system. Finkelstein has stated correctly that

eclampsia and other severe nervous symptoms that occur during the eruptive days of hereditary syphilis, may be due to a temporary outpouring of hydrocephalic fluid. In favor of this view are, the increased tension in the fontanelle that is out of all harmony with the miserable condition of the child, and the increase of pressure as shown by lumbar puncture. The latter reveals a perfectly clear cerebrospinal fluid.

Besides this internal serous meningitis there occurs in infants with hereditary syphilis a *pachymeningitis hæmorrhagica*. There are further inflammatory changes in the brain and meninges, diffuse and circumscribed, and specific vascular lesions with resultant tissue changes, that cannot be discussed at length in this connection. This fact, however, deserves mention, that hydrocephalic enlargements can result in hereditary syphilis, from these conditions. If hydrocephalus is accompanied, for a long time, by manifestations of paralysis, or of contractures, then, in all probability, there is underlying it a complicating brain lesion.

The experience that a great number of cases of hydrocephalus in childhood are due to syphilis, as a result of true or parasyphilitic changes, makes it a duty to use antisyphilitic treatment in every case. As a matter of fact it is possible, in a great many cases, to cure recent cases of hydrocephalus by this treatment, and to prevent others from developing.

Fig. 132.



Syphilitic hydrocephalus with a high degree of engorgement of the veins of the scalp and with a well marked nasal deformity (pug-nose).

Neuritis involving the peripheral nerves does not seem to occur in early hereditary syphilis.

Clinical manifestations of involvement of the spinal cord in early hereditary syphilis have not been observed hitherto; and yet anatomical findings are admitted by Gilles de la Tourette and Gasne, who found diseased vessel walls and interstitial cell proliferations, as well as diffuse involvement of the spinal meninges, in both newborn and older infants with hereditary syphilis. The observations by Peters of specific spinal paralysis are more than doubtful. The findings of Sibelius, on the other hand, deserve consideration; he found developmental disturbancs in the cells of the spinal ganglion in newborn syphilitic children.

Ocular Affections.—Syphilitic affections of the eyes are observed even in the newborn in the form of a plastic iritis which may run its course within the uterus and may lead to synechia of the iris. Iritis of

early hereditary syphilis runs its course without the violent inflammatory manifestations that ordinarily go with this affection. A diffuse optic neuritis may occur during the first few months; still more frequently however a chorioiditis with the formation of peculiar spots. On the other hand the parenchymatous keratitis of late hereditary syphilis is very rare in the early form. It must be remembered further that in the newborn, traumatic changes brought about during birth, especially inflammatory processes of the uveal tract, may occur, which may easily be confused with syphilitic lesions.

The *organ of hearing* seems to be involved only exceptionally in a specific manner in infantile syphilis, although a discharge from the ear does occur in some of these cases.

Affections of the Lymph-nodes.—The torpid polyadenitis characteristic of acquired syphilis has its analogy in early hereditary syphilis

Fig. 133.

Syphilitic hydrocephalus. A high degree of atrophy. Saddle-nose with the end of the nose retracted. Borders of the lips infiltrated.

in the frequent but by no means constant appearance of general glandular enlargement during or soon after the period of eruption. If one examines carefully the inguinal and axillary regions of somewhat older infants with hereditary syphilis it is not difficult to make out a definite slight glandular enlargement. It is a much more important fact, however, that glandular bodies appear in infants with early congenital syphilis in places in which normally no glands are palpable, as in the cubital region, and in the fourth or fifth intercostal space at the side of the thorax. Regional glandular enlargement that is not dependent upon *ulcerated skin lesions*, but in extremities that are the seat of bone involvement may also occur. In all of these conditions of glandular enlargement we have only a very moderate enlargement; rarely do these lymph-nodes become larger than a bean. In the glandular enlargement of the relapses of the second to the fourth year when they are associated with condylomatous efflorescences there is a very diff-

erent condition. Here we have, at times, lymph-nodes that attain the size of hazel-nuts with no tendency to suppuration.

Complicating Diseases During Infancy.—Congenitally syphilitic

Fig. 134.—Advanced hydrocephalus (balloon head) in an eight months' child with hereditary syphilis. Multiple syphilitic thickenings of the bones at the diaphyseal ends.

infants have a very marked predisposition to septic infection. The cause of this lies in the many chances for infection due to the purulent rhinitis and the rhagadic ulcerations at the various openings into the body. It is not necessary, in explaining this tendency, to resort to the

idea of physical inferiority and lack of resistance of the tissues brought about by congenital syphilis, when the avenues for infection are so extraordinarily numerous. It is not difficult to explain the frequent lung affections of the syphilitic newborn as affections due to a purulent nasal secretion that runs downward, or the frequent skin and periarticular suppuration as due to metastases from various primary foci of suppuration.

A frequent complication is found in *pseudofurunculosis* to which especial attention must be drawn because of the fact that the flaccid abscesses that occur in this condition are frequently considered gummata. Besides these exogenic infections of the subcutaneous tissue there occur also in the skin of congenitally syphilitic children true cutaneous furuncular infiltrates and pustules as a part of a severe general pyæmia. Frequently this septic secondary infection in syphilitic children manifests itself as a hæmorrhagic disease of the newborn, in which there occur melæna, purpura and bleeding from the umbilicus. For a long time a specific vascular lesion was erroneously thought to be the cause of this phenomenon and a special form of *syphilis hereditaria hæmorrhagica* was thought to exist.

When occasionally the eruptive lesions of early hereditary syphilis show a hæmorrhagic character this can doubtless be attributed to changes in the vessel walls, but these do not explain fœtal internal and external hæmorrhages accompanied by general dissolution of the blood. In these cases there is always a secondary septic infection which can produce hæmorrhagic disease in the syphilitic newborn child as well as in the healthy one. Hess distinguishes three forms of disease in this so-called hæmorrhagic syphilis of the newborn: (1) hæmorrhagic disease without evidence of syphilis, but with syphilitic ancestors—an exclusively septic infection; (2) the same, but in children who are manifestly syphilitic; (3) severe, evident, congenital syphilis with severe internal and external hæmorrhages.

A very frequent complication of early hereditary syphilis is found in purulent synovitis of the larger joints which is not infrequently associated with periarticular abscess formation.

Parasyphilitic Affections.—According to A. Fournier we have here tissue changes whose final cause is to be found in a syphilitic infection but without the real products of syphilis, *i.e.*, real syphilitic lesions.

These affections are uninfluenced by specific treatment with either mercury or iodides. They are divided into organic affections that are well characterized anatomically, and functional disturbances of widely different kinds without any demonstrable anatomical ground.

Hallopeau has recently proposed the term "syphilitic deuteropathies" for these changes. Tommasoli and La Mensa designate as "syphilismus" the constitutional disturbances in the offspring caused by the depraved generative cells of syphilitic individuals.

If individuals who present genuine manifestations of syphilis in the earliest period of life, show evidence of parasyphilitic diseases later in life, this is not hard to understand and is not to be distinguished from the corresponding conditions present in acquired syphilis. And yet many authors consider that parasyphilitic symptoms may appear in infancy and childhood as the sole manifestation of syphilitic influence upon the offspring from an infected ancestor, without such children having ever shown genuine virulent manifestations of syphilis. This influence they think may extend even to the third and fourth generations (grandchild and greatgrandchild).

Among the parasyphilitic manifestations the following are the most important: anæmic and atrophic conditions, failure to gain in weight and to develop properly, as well as fœtal cachexia. A depraved condition of the generative cells of the parent due to the action of the syphilitic toxin is held responsible for these conditions, much as in the offspring of a tainted parent we see the effects of alcoholism, tuberculosis, saturnism, mercurialism, nicotism, etc. And yet there is little real evidence in favor of such an influence, since one can always assume organic changes in any part of the body during fœtal life and one can think of these dystrophic conditions as resulting from them. Finger's important hypothesis that makes a distinction between purely toxicogenic and bacteriogenic syphilitic manifestations explains the general inferiority of the tissues of hereditary syphilitic children as a result of the action of toxins.

A further division into meta- and parasyphilitic affections is frequently made. In the first class would belong anatomically well characterized organic changes, that have a syphilitic base, such as, especially, the changes in the central nervous system (Möbius): tabes, dementia paralytica, hydrocephalus, cerebral paralysis of childhood, etc.; to which others would add also spastic hemiplegia and diplegia. In the second class would belong the general disturbances of development of the heredosyphilitic, among which one would consider diabetes mellitus and insipidus, as well as the hæmoglobinuria of hereditary-syphilitic children.

It is not necessary to assume a harmful parasyphilitic protoplasmic change to explain the constitutional disturbances that occur during the eruptive period of early hereditary syphilis and that are characterized by pallor and stationary weight. Severely affected, atrophic, syphilitic children are never free from visceral and osseous manifestations, so that the cachexia in these cases can be directly attributed to the functional disturbance of organs that are important to life. The irritation of the bone marrow which is never absent, and which is characterized by the pouring out into the blood of characteristic leucocytes (myelocytic anæmia) is also of significance in this connection. It has, therefore, by

no means been proven that the high mortality of hereditary-syphilitic infants is due to any peculiar tissue inferiority. Still, the influence of fœtal syphilitic inflammatory processes on the one hand, and the disturbances of blood formation and the septic secondary infections on the other, sufficiently explain, in themselves, the high mortality of syphilitic children.

4. SYPHILITIC RELAPSES IN EARLIEST CHILDHOOD

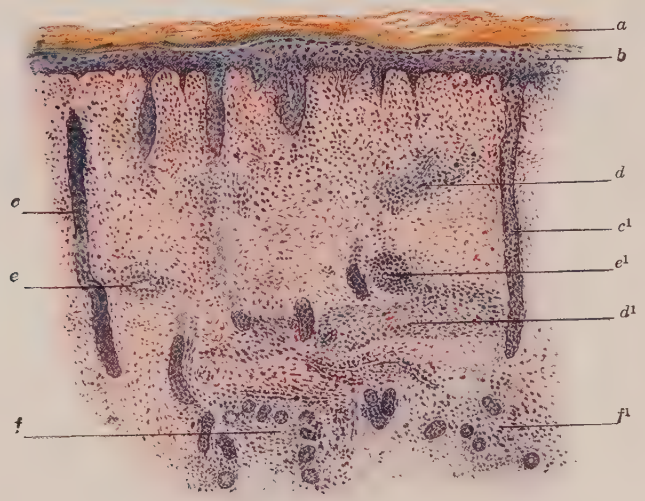
Inasmuch as the first manifestations of syphilis, in a great many hereditary-syphilitic children, run their course within the uterus, the whole period of infantile syphilis and the first eruption are a relapse in many cases. It is enough to mention in this connection the visceral, osteochondritic and nasal lesions that start during intra-uterine life and are frequently not followed hy an eruption until after birth. But even after the first eruption, no matter whether this is part of the first appearance of the disease or not, relapses occur during infancy in the most widely different organs. Frequently these manifest themselves as a continuous progressive development, without any periods of latency, and advance until a large number of organs are affected. We find, for example, that certain affections of the bones are frequently associated with the first period of skin eruption, especially those of the small hollow bones (phalangitis) and the periostitis of the cranial bones with its tendency to hyperostosis. The collection of hydrocephalic fluid often goes hand in hand with these. Not infrequently the first exanthem is followed by an unbroken series of different skin lesions, such as recurring infiltration in the lower half of the body, gumma formation, oozing condylomata, and mucous patches. Involvement of the organs of special sense likewise occurs. In general the following statement is true: the further a child has passed beyond the period of infancy, the less do cutaneous lesions manifest themselves.

Not infrequently congenital syphilis recurs even during the period of infancy in the form of affections of the *central nervous system*, especially as cortical encephalitis the result of specific vascular lesions, and as hydrocephalus. A number of these cases run their course as a cerebral paralysis of childhood with or without epileptic attacks, and are later accompanied by disturbances of intelligence. It is an important fact that syphilitic brain diseases may occur in infancy without evidence of a preceding exanthem; and that the striking result of the use of antisyphilitic treatment in many affections of the brain accompanied by epileptic seizures in earliest childhood, reveals the syphilitic origin of the disease.

Ocular lesions, either independently, or in specific combination with other syphilitic lesions due to relapses are much more frequent toward the end of the period of infancy than during the first period of

PLATE 29

I.



II.

I. Vertical section through the sole of an eight-weeks-old syphilitic child with diffuse plantar syphilis.

a, flattened epidermis; *b*, rete Malpighii slightly swollen. Between *a* and *b*, stained green, is the stratum lucidum; *c*,*c*¹, glandular ducts; *d*,*d*¹, round-cell infiltration around blood-vessels; *e*,*e*¹, cross-section of blood-vessels, increase of adventitious and periadventitious layers; *f*,*f*¹, pathological cell-growth and vasculitis around the sweat glands and ducts.

Stained after Unna with polychromous methylene blue and orcien. Stratum corneum, yellow; stratum lucidum, green; rete mucosum and gland-ducts, light violet; cell-nuclei, dark violet blue; mast-cells, cherry-red.

II. Diffuse infiltration of soles of feet in a two-months-old infant with hereditary syphilis.

III.

a. Papuli crustaceous syphilid. *b* and *c*. Pemphigus syphiliticus.

eruption. Above all others in importance in this connection is the focal *choreoretinitis* of Hirschberg, which is most characteristic of syphilis present at birth but which also appears during later relapses. Of less significance in the relapses of earliest childhood are indurative lesions of the palpebral cartilages.

Involvement of the testicle during the period of infancy is another form of relapse in congenital syphilis. There is here a diffuse interstitial cell proliferation analogous to the diffuse process in the liver (Hutinel). This manifests itself clinically by enlargement and indolent hardening of the organ (Henoch). Since this lesion, nearly always bilateral, is accompanied by no particular subjective symptoms it frequently escapes notice unless it is looked for as a matter of routine in the cases of infantile syphilis. The epididymis always remains free. Syphilitic orchitis of infancy never leads to suppuration and is a peculiarly favorable lesion from a standpoint of therapeutics. The relapse manifestations of congenital syphilis during infancy are by no means exhausted by those organic changes that have been enumerated so far. Especially frequently are the viscera (liver, kidneys, pancreas) involved. The thymus also may be affected, at times becoming very large and thus producing, as Marfan and I have observed, stenosis of the trachea with stridor thymicus; the latter disappearing promptly under antisyphilitic treatment. Paroxysmal hæmoglobinuria and hæmatoporphyrinuria, of syphilitic origin, may occur in infancy.

Quite imperceptibly at times, relapses of congenital syphilis extend into the second and third year of life, localizing themselves especially in the skin, in the visible mucous membranes, and in the osseous system.

The most important *skin lesion* of hereditary syphilis of the second to the fourth year of life are condylomata lata of the genito-anal region; these differ in no way from those of acquired syphilis.

The visible mucous membranes frequently show, even up to the sixth year of life, syphilitic recurrences in the form of mucous patches, the favorite location of which is the mucous membrane of the mouth and pharynx including the tonsils, but especially the upper surface of the tongue. On the latter, extensive manifold condylomata with a tendency to repeated recurrences are not infrequent (Plate 27).

Recurrent exanthemata occur, but rarely, up to the middle of the second year of life, either in the form of an extensive eruption of prominent papules at the hairy margin of the forehead or on the flexor surface of the extremities, or in the form of inconspicuous, tender, half-lentil to bean sized spots on the forehead and the lower part of the body; these are at first salmon colored, later yellowish, shining, and somewhat scaly. The trunk is nearly always entirely free.

Exanthemata of this latter variety usually occur only after insufficient treatment of the first symptoms of syphilis; they very closely

resemble the eruptions of herpes tonsurans maculosus and are frequently overlooked or misinterpreted. Occasionally there are found, even during the second year, on the skin of the extremities and of the back, small, disc-shaped, lightly pigmented spots, not raised above the surface, which take on a bluish violet tint and become clearly marked when the child cries.

Toward the end of the first and during the second year there frequently develops the clinical picture of pseudoleukæmic anæmia with marked splenomegaly, so that the spleen occupies, as a hard body, the whole left half of the abdomen and may reach down into the pelvis. The liver is always considerably enlarged at the same time. In many cases of hereditary syphilis with hepatic and splenic enlargement the liver is much larger than the spleen. Here there is a real syphilitic involvement of the liver with an indurative hyperplasia of the spleen, while the type first described is a manifestation of pseudoleukæmic anæmia, an affection that may occur without preceding syphilis, especially in severe rickets.

Fig. 135.

Larynx of a fifteen-months-old child with hereditary syphilis. Growing condylomata on the epiglottis and false vocal chords. Complete aphonia.

After the period of infancy, congenitally syphilitic disease of the visceral organs often takes on a true gummatous character in the form of solitary syphilomata, which may occur both in the parenchymatous and lymphatic organs and the mucous membranes. A nodular appearance of the liver is very frequent. Contracted kidney as a result of syphiloma likewise occurs during childhood.

The skin and subcutaneous tissues occasionally show solitary gummata in the years following infancy. These appear as fluctuating, dome-shaped projections, in size from that of a bean to a hazel-nut, with or without slight reddening, and unaccompanied by fever. If recognized early and treated with mercury these rapidly disappear. If not, they burst and empty out a tough, sticky, light yellow mass and are converted into cup-shaped, thick-walled ulcers that are painless and without reaction and heal with great difficulty even under the most approved treatment.

A rare form of recurrence is to be found in a diffuse, sclerotic glossitis, which von Düring has observed repeatedly in endemic syphilis and which I have seen three times. The tongue is either enlarged in toto, projecting from the mouth, much as in myxœdema, the whole muscular portion being uniformly thickened but the tongue not being

œdematous or painful; or there may be large circumscribed nodules that occupy from one-third to three-fourths of the whole parenchyma of the tongue. Such indurations of the tongue occur during childhood only with syphilis.

Laryngeal involvement is an important manifestation of recurrence of hereditary syphilis. According to Ripault there are usually present nodular, papular growths on the epiglottis and the mucous membrane of the vocal cords, that break down into ulcers, and later form scar tissue. We ourselves have seen the surface of the vocal cords and epiglottis thickly covered with condylomata in a child of 15 months with hereditary syphilis (see Fig. 133).

Laryngeal syphilis of earliest childhood often presents the picture of croup and is often mistaken for croup; in some cases intubation and tracheotomy have been performed to prevent suffocation. Hereditary laryngeal syphilis is comparatively rare during the third and fourth years, but becomes more frequent again during the period of late syphilis. The essential symptom is hoarseness, even complete aphonia, without a demonstrable catarrhal condition of the deeper air-passages.

5. LATE HEREDITARY SYPHILIS

By late hereditary syphilis we mean all organic affections of later childhood and of adult life, that are caused by hereditary syphilis and that are analogous to the teritary manifestations of the acquired form. Age is of less significance here than the peculiar manifestations of syphilis; the gumma being the foundation of late hereditary syphilis. As a rule gummatous processes in hereditary syphilis do not arise before the fifteenth year, but when they occur earlier, as they do exceptionally, even in the third and fourth year, they must be classed nevertheless as manifestations of late hereditary syphilis. (See Recurrences in Early Childhood.)

There are authors who still believe in the possibility of a latent period in hereditary syphilis to the time of puberty, and who consider only such cases as late hereditary syphilis in which tertiary symptoms have not been preceded by early manifestations of syphilis during the first few years of life. There are no plausible grounds for assuming such an outbreak of tertiary symptoms alone. In children who apparently have late hereditary syphilis alone, early manifestations may have been overlooked because of the possible absence of eruptions, or there may have been a contact syphilis that ran its course early in childhood and escaped observation.

As the extreme age at which condylomatous recurrences may take place in hereditary syphilis I would designate the sixth year, during which year I have still found condylomata of the mucous membrane. As a rule these do not occur even after the fourth year.

In late hereditary syphilis, genuine syphilitic manifestations are much more sharply distinguished from parasyphilitic affections than in the early period of the disease, these parasyphilitic manifestations involving especially the central nervous system in the form of tabes and paralytic dementia. Late hereditary syphilis frequently appears first during the period of second dentition or during puberty.

We will now discuss briefly in the order of their frequency the lesions of the different organs involved in late hereditary syphilis.

First are affections of the eye which will only be mentioned, leaving their detailed discussion to the oculist. Here belong parenchymatous keratitis, gummatous involvement of the iris and the so-called deep inflammations of the eye, choreoretinitis and optic neuritis.

Very frequently ocular and aural lesions appear at the same time, but the latter usually occur later. When the ears are affected, there is rapid, usually bilateral, deafness. It occurs much more frequently after puberty than before and is accompanied by symptoms of dizziness and subjective noises. Deafness is due to *neuritis acustica* (Menière's disease).

Late syphilitic changes in the osseous system take place, either as a diffuse hyperplastic ostitis and periostitis, or as a gummatous process; both lesions, however, may occur not only simultaneously in the same individual but also in the same bone.

The hyperplastic ostitis and periostitis may involve the whole skeleton (Lannelongue) and may cause visible swellings of the cranial bones as well as of the long hollow bones (see Plate 30). And yet hyperplastic processes in the cranial bones occur incomparably less frequently in late than in early hereditary syphilis. The long hollow bones are most frequently affected, especially the shinbones, their involvement in late hereditary syphilis forming an extremely characteristic clinical picture. In general, all of the bone lesions of tertiary acquired syphilis occur also in late hereditary syphilis. Lannelongue considers the so-called Paget's bone disease, which is a diffuse, progressive periostitis leading to hyperostosis and finally affecting the whole skeleton, as nothing more than hereditary bone syphilis.

As mentioned above, the tibia is the bone most frequently involved. There occur at first on the crest of the tibia rather soft and very tender swellings. The skin over these areas is frequently slightly reddened and sensitive. At the same time there is frequently spontaneous pain in the lower extremities increased decidedly on attempting to move them. The first stage of the affection during which new tophi appear one after the other on the edge of the tibia, may last for months or may progress so rapidly that they resemble *erythema nodosum*. The second stage is the real stage of hyperostosis. The entire shin becomes swollen, thickened, and the sharp edge of the bone disappears. The anterior

border of the bone becomes rounded and is covered with palpable hard nodules and rough areas. The whole bone is diseased. Anatomically this deformity is due to the continuous formation of new periosteal bone layers about the primary bone. Even the hollow portion of the bone is, in many cases, obliterated for considerable distances and is filled by compact bone substance. The tibia is frequently bent, with marked anterior convexity, the bone assuming the shape of a Turkish sabre; or, if the ossifying periostitis of the anterior margin of the tibia far exceeds that of the other surfaces, we have the sabre sheath deformity of Hutchinson and A. Fournier (see Plate 30).

Among the less frequent bone changes in late hereditary syphilis is a rarefying periostitis leading to bone absorption. This occurs occasionally on the surface of the cranial bones and may lead to extensive resorption of bone with the formation of rough areas on the surface (*caries sicca*).

Just as in the tertiary stage of acquired syphilis, there occur at times in late hereditary syphilis nodular periosteal swellings (gummata) with their favorite location again in the tibia, but also in the bones of the upper extremity, the cranium, and the sternum. These are at first rather soft, sensitive swellings that are surrounded by a wall of hyperostosis. They either heal, leaving a depression, or discharge and become converted into thick walled, excavated ulcers which heal with the formation of adherent scars. If the gummatous process is centrally located, bone necrosis may result.

The short hollow bones, too, may be involved in late hereditary syphilis, but these lesions no longer show a typical course with preference for the first phalanges of the fingers, but occur without any definite rule in the phalanges, carpus, and bones of the foot.

The lesions of the nose and of the alveolar processes show no differences in acquired and in late hereditary syphilis. Perforations of the bone that are rare in early syphilis, are of frequent occurrence at this stage.

Not infrequently, hereditary syphilis leads to lengthening of the affected long bones in older children. This is especially striking in the occasional lengthening of a lower extremity, like a partial gigantism, in which the affected bones become plump and rougher. Frequently such bone changes are preceded for months, even years, by severe nocturnal headaches.

In late hereditary syphilis genuine *syphilitic joint lesions* of a very definite type occur. The knee-joints are most frequently involved, at times, even during youth and adult life. According to my experience two main types can de distinguished:

1. *Joint affections without involvement of the bone and cartilage.*— These naturally fall into two subdivisions: (*a*) simple hydrops of the joints without material thickening of the joint capsules,

the synovial membranes and the tendon sheaths; running an afebrile, almost painless course; it is almost exclusively limited to the knee and ankle-joints and causes a slight feeling of weariness and weight in the legs; (*b*) hyperplastic synovitis. In this form the joint capsule, the synovial membranes, together with the tendon sheaths, are all thickened and almost gelatinous. Friction rubs can usually be heard and felt in these joints. This process may involve the phalangeal and carpal joints, then the smaller joints of the foot, in fact may spread to every joint in the body, including those between the vertebræ, as a generalized hyperplastic arthromeningitis.

2. *Joint affections with enlargement of the ends of the bones.*— These likewise fall into two subdivisions: (*a*) combination of hydarthrosis with swelling of the joint ends of the hollow bones. This is the most common form of joint affection in late hereditary syphilis, resembling not a little the clinical picture of arthritis deformans. It is important from a diagnostic standpoint that the swollen bone ends are not sensitive to pressure. The Röntgen ray, too, shows there no periosteal layer formation as in the affections of the diaphysis; (*b*) an affection simulating white swelling. This is usually monarticular, painful, and is associated with limitation of motion, like the tuberculous form. It may lead to rupture and to necrosis.

It is especially important for the pediatrist to be able to distinguish between tuberculous, or scrofulous, and syphilitic bone and joint affections. In general, caries is more frequent in tuberculosis than in hereditary syphilis. The syphilitic bone affections are less tender than those due to tuberculosis and produce fewer functional disturbances. In bone syphilis of later childhood, too, there is an absence of hectic fever and of the profound cachexia of bone tuberculosis. In the cases that go on to suppuration the nature of the skin involvement may lead to a differential diagnosis. The peculiar character of the skin in scrofulous caries, the violet discoloration, the manner of perforating, the formation of multiple fistulas, and the spongy granulations, all speak unqualifiedly for tuberculosis and are absent in syphilis.

In case of bone swelling without suppuration the localization is of some importance. In general the cranial bones are more prone to syphilis than to tuberculosis, and especially the frontal and parietal bones, particularly their eminences. Only the temporal and malar bones are more frequently the seat of tuberculosis than of syphilis. Affections of the occipital bone again are as a rule syphilitic in children.

The skin lesions of late hereditary syphilis differ in no way from the tertiary skin lesions of acquired syphilis. According to my experience there are two main forms of true skin lesions: the small nodules, and the large nodular late syphilides. In the former they are circumscribed infiltrations of the skin that feel hard at first and vary in size from a split

pea to a lentil. The skin over these nodules becomes brownish in color and either desquamates or becomes covered with a crust. These nodules are usually grouped together closely, very much as in lupus vulgaris. Below the crusts the granulation tissue disintegrates, while the crust itself grows larger and assumes the shape of a cup, or of an oyster shell. Some nodules may undergo resorption. In general these late small nodular syphilides show a serpiginous arrangement.

This serpiginous syphilide of childhood belongs to the most intractable manifestations of syphilis, from a therapeutic standpoint.

The large nodular syphilide occurs in the form of large skin gummata, and gummatous ulcers, though not a frequent lesion. The point of origin is usually the subcutaneous tissue.

The mucous membranes also, especially those of the respiratory tract become invaded in a specific manner in late hereditary syphilis. It is not always possible to determine whether the gummatous process, in this case, starts in the mucous membrane itself or in the deeper lying tissues. This is especially true of the lesions of the nasal and pharyngeal mucous membranes. In older children the differential diagnosis between ulcers of the skin and mucous membranes due to tuberculous lupus on the one hand and those due to syphilis on the other hand, are to be considered. Rapidly progressive ulceration with absence of nodular infiltration always speaks for syphilis. Pharyngeal and laryngeal ulcers due to hereditary syphilis are characterized by sharply defined borders and by thick walls.

As far as the nose is concerned, a diffuse osseous and periosteal affection of the whole nasal skeleton, or the formation of gummata within the cartilaginous or bony nasal septum or at the base of the nasal cavity, may represent the primary pathological process; breaking down of the affected tissues may be followed by ulceration of the mucous membrane. And yet circumscribed nodules may form on the mucous membrane of the cartilaginous and soft portions of the nose and these may lead to ulcer formation. Probably the most frequent lesion is a gummatous ostitis of the bony portion of the septum, the first symptom of which is an obstinate nasal obstruction. The gummatous ulceration is always accompanied by much pus and crust formation. If proper therapeutic measures are not instituted at the right time, deep ulceration will take place with perforation of the septum, or the floor of the nose, together with necrosis of the affected portions of the ethmoid and the superior maxilla. The final outcome of such nasal disturbances will be discussed in connection with the discussion of the stigmata of hereditary syphilis.

Atrophic rhinopharyngitis, or ozæna, is a frequent syphilitic deuteropathy in children between six and fifteen years of age. The smooth atrophy of the base of the tongue (Levin, Heller) characterized

by smoothness and thinness of the mucous membrane and by absence of glands, likewise occurs as a luetic deuteropathy in children of the above-mentioned age with hereditary syphilis.

The palate and pharynx become invaded very frequently and in a very characteristic manner in late hereditary syphilis. I would mention first the syphilitic tophus of the hard palate, usually projecting from the raphe, a lesion which contrasts strongly with the purely mucous membrane affections of hereditary syphilis on account of its painful character, and which represents a stage preceding ulcerative palate perforation. Furthermore, gummata occur on the velum palati and within the palatine arches, and may lead to deep ulceration and perforation. The favorite location is the point of insertion of the uvula and the middle portion of the anterior palatine arch, where at first painless swellings arise. These reveal their presence only by a slight peculiarity in the voice sounds such as exists with a tonsillar abscess, but they do not materially interfere with swallowing. Not until ulceration or perforation has taken place do we notice the well-known functional disturbance of speech and swallowing.

Circumscribed or diffuse swellings arise also on the mucous membranes of the epiglottis and of the larynx that are of great importance because of their interference with speech and respiration. The late syphilitic ulcers of the nasopharynx, larynx and trachea have a decided tendency to the formation of scar tissue with contractions. For that reason, very characteristic sequelæ of late hereditary syphilis are such lesions as cicatricial adhesions of the velum palati to the posterior pharyngeal wall, contractions and distortions of the epiglottis, stenosis of the larynx and of the trachea, the latter being among the most serious lesions from a therapeutic standpoint.

Among the visceral lesions of late hereditary syphilis, so far as frequency is concerned, liver affections deserve the first rank, although the lesions differ in no way from those occurring during tertiary acquired syphilis. The large nodular gumma, the diffuse connective tissue hypertrophic cirrhosis, and the characteristic lobulated liver, resulting from a combination of these two conditions, deserve mention. These liver changes are always associated with hyperplasia of the spleen.

Many cases of contracted kidney and of amyloid degeneration of the kidneys may be a manifestation of late hereditary syphilis. It is certain also that diabetes insipidus in infants is frequently associated with hereditary syphilis.

Lesions of the circulatory apparatus in late hereditary syphilis will be discussed in the chapter on diseases of the circulatory system. It should be mentioned, however, in this connection, that gummata aortitis, as well as arteriosclerosis and phlebosclerosis, occurs in congenitally syphilitic children, and that the presence of the latter condi-

tions during childhood always justifies the diagnosis of syphilis. Myocardial and endocardial changes are observed in late hereditary syphilis.

Hyperplasia of the adenoid tissue in the nasopharynx is a very frequent finding in hereditary syphilis, without however having any peculiar characteristics that are of diagnostic value. Not alone is Luschka's tonsil hypertrophied, but also the remainder of the adenoid ring of the throat, the tonsils, and the adenoid tissue at the base of the tongue. In the latter position two diametrically opposite conditions can exist: a smooth atrophy, and adenoid hypertrophy.

On account of the great frequency of adenoid vegetations in the nasopharynx in older children with hereditary syphilis, there are nearly always present enlarged submaxillary and cervical lymph-nodes. Naturally, these must not be looked upon as a specific adenopathy, although such a condition can exist in late hereditary syphilis. There is a certain tendency to glandular enlargement even in these older syphilitic children, so that lymph-nodes can be felt in places where there are none palpable normally, as for example, in the cubital region [epitrochlear lymph-nodes.]

Besides these simple lymph-node hypertrophies, there occur though not frequently, genuine gummata of the lymph-nodes. This may take one or two forms: either an enlargement of a single node, or group of nodes, that are hard and painless and have but little tendency to softening; or as a generalized lymph-node hypertrophy, very simliar to the polyadenitis of the secondary stage of acquired syphilis, except that in the late hereditary syphilis of childhood the nodes become larger than in the other condition.

If these are only isolated enlarged lymph-nodes, the differential diagnosis from tuberculous lymphadenitis is not always easy. As a rule stigmata of syphilis are present in the one case, and help in making a diagnosis. The more marked appearance of periadenitis in the syphilitic form is of some diagnostic value. The course of suppuration of a gummatous node is wholly different from that of a tuberculous node. In the breaking down of a gummatous node a circumscribed portion of the swelling unites with the skin and the latter breaks down rapidly over a considerable area, giving rise, after the emptying of the characteristic contents of the gumma, to an ulcer with all of the characteristics of the syphilitic type. The gummatous involvement is exceedingly amenable to antisyphilitic treatment, a fact that is of great value from a diagnostic standpoint.

Hereditary syphilis frequently causes general nervous disturbances, even a nervous predisposition. Many of these children are feeble-minded. Difficulty in learning and in observing, and attacks of night terrors are frequently attributed to adenoids in the nasopharynx, but operation in these cases leads to no improvement and shows that there is some more

fundamental cause. Psychoses, too, occur in these children at the time of puberty (Dornblueth). To this period belong infantile tabes and progressive paralysis, while epilepsy of the Jacksonian type is possible at any time during childhood, superimposed upon the same syphilitic foundation. These diseases, together with brain and spinal syphilis of the second period of childhood, and the pseudotabes of hereditary syphilis, are all discussed in their appropriate place in that part of this work that deals with diseases of the nervous system.

Stigmata of Hereditary Syphilis.—In a great many cases hereditary syphilis leaves lasting changes by which it can be recognized. These are especially well marked during the second period of childhood, while some of them may disappear during later life. These stigmata consist of general disturbances of development, of cutaneous scars, of certain skeletal changes, and of the so-called Hutchinson's triad.

1. *General disturbances of development* are especially significant at the time of puberty, because infantilism is frequently observed with dwarfism and retarded sexual development. This infantilism occurs as a sequel to severe early hereditary syphilis from which the child recovered in earliest infancy and is distinguished from dwarfism due to other causes by the invariable presence of other unmistakable manifestations of syphilis.

2. *Scars.*—The ulcerative skin affections of hereditary syphilis leave scars, the location and configuration of which frequently make possible a retrospective diagnosis of hereditary syphilis, without any knowledge of its previous manifestations. The radially arranged circumoral, circumnatal and circumanal scars and the scar formations on the mucous membranes of the palate, pharynx, and larynx are very significant. The most important scar symptoms are the radially arranged cicatrices on the lips which give the latter a generally paler and wrinkled appearance.

3. *Skeletal Changes.*—The bone changes of the first few years, as well as those of later childhood, leave permanent bone deformities. Among these are peculiar deformities of which Parrot's natiform caput has been mentioned repeatedly. There is present a thickening of the frontal and parietal eminences and a broadening of the transverse diameter of the skull, so that there is formed a more or less deep furrow, not unlike the intergluteal fold. Frequently, too, there is associated a prominent bulging forward of the whole abnormally high broad forehead with especially marked projecting and rounded eminences, the so-called "Olympic brow." There are observed also cranial asymmetries, that are not however, always to be attributed to syphilis, but rather to a cranial hyperostosis of syphilitic origin combined with rachitic changes. Hydrocephalic and microcephalic heads, likewise, are found as a result of hereditary syphilis. Permanent deformities of the nasal skeleton are frequent,

such as pug-nose, saddle-nose and lorgnette nose. The first anomaly is characterized by flattening and broadening of the base of the nose immediately below the place where it leaves the frontal bone. The second anomaly consists of a sinking in of the nose with a retraction of the end, together with an upward direction, so that the axes of the nostrils extend diagonally forward and upward. In the lorgnette nose (A. Fournier) the lower nasal segment is uniformly depressed and seems to come out of the upper segment, much like the oculars of an opera glass.

Further permanent deformities are found in the shinbones in the form of thickening and tuberosities of the crest of the tibia, and in the form of the sword-sheath shaped tibia already mentioned.

4. The so-called *Hutchinson's Triad* is a group of symptoms, composed of changes in the teeth, eyes, and ears. In the eyes of older children with hereditary syphilis there are frequently found leucoma, spots, and opacities of the cornea, as a sequel to a parenchymatous keratitis; also changes in the iris, such as synechiæ and irregular pupils; as well as the spots on the chorioid that are characteristic of former hereditary syphilis. The history usually discloses the existence of some ocular trouble dating from earliest childhood. With reference to the ear one frequently obtains the history of an early discharge from the ear or, in some cases, of partial deafness without discharge. Very characteristic is a sudden deafness due to neuritis of the auditory nerve. The drum membranes may show a great variety of changes.

It must be remembered that *with the exception of sudden deafness,* these lesions of the organs of special sense are not pathognomonic of hereditary syphilis. Parenchymatous keratitis, especially, which is usually justly attributed to hereditary syphilis is also found rarely in other than syphilitic children, particularly in those that are debilitated from other causes, such as tuberculosis. No diagnostic value can be attached to those stigmata referable to the organs of special sense, unless there is present other evidence of past hereditary syphilis.

The same is true of *Hutchinson's teeth,* an anomaly found exclusively in the upper central incisors of the second dentition. Typical Hutchinson's teeth always show a single, rather superficial, crescenting, broad notch in the middle of the lower border, with rounded corners. In most cases the dentine is laid bare in the centre of this crescentic notch, due to a defect in the enamel; this defect is not, however, by any means, a constant accompaniment. Not rarely one finds these upper central incisors either inclining toward or away from one another; but rarely are they long enough to touch the adjacent teeth. This deformity certainly does occur in children with hereditary syphilis and Hutchinson's explanation for this anomaly, *i.e.,* a nutritional disturbance of the dental germ due to syphilis, is doubtless correct. But this same harmful influence that syphilis has upon the dental germ can be excited by

all kinds of acute and chronic infections and constitutional diseases if they appear before the eruption of the permanent teeth. Thus, both Welander and I have seen Hutchinson's teeth in individuals who were positively free from syphilis, and also in children with early acquired syphilis.

With reference to all of these stigmata, it may be said that those alone have indisputable diagnostic value that are the result of actual past specific lesions, such as the scars on the skin and mucous membranes and certain bone and eye anomalies; but that many other alleged stigmata, such as discharge from the ear, partial deafness, corneal opacities, and dental anomalies, occur likewise with other diseases that are accompanied by general weakness and lowered resistance of the youthful organism. *An absolutely positive proof of former hereditary syphilis is found in the radial scar formation on the lips.*

Hutchinson's triad doubtless occurs frequently in hereditary syphilis; but it is not a positive proof of the existence of that disease. It must be mentioned, further, that in children who are properly treated in infancy these questionable symptoms, especially that referable to the teeth, only exceptionally occur.

6. DIAGNOSIS OF HEREDITARY SYPHILIS

We have learned to recognize the great diagnostic value of the Rontgen ray examination of the long bones in fœtal syphilis, since Wegner's osteochondritis can easily be recognized, provided the fœtus belongs to the second half of pregnancy.

Wassermann described a biologic test for the diagnosis of syphilis in 1906 which is now considered one of the most important diagnostic aids in the detection of this disease. The *Wassermann reaction* is of great importance in the diagnosis of hereditary syphilis, latent syphilis in children and for syphilitic nerve disorders. The reaction depends on the following biologic principles: When a solution of the red blood corpuscles is mixed with the serum of an immunized animal the hæmoglobin is set free and the solution becomes pink in color. This is termed *hæmolysis*, and depends on the action of two distinct serum factors. One is termed *amboceptor*. This can be produced in the serum of animals by means of repeated injections of foreign cells. The amboceptor is characterized by its specificity. The other is termed *complement* and is always present in fresh serum but disappears gradually on standing or is destroyed by heating at 56° C. If red cells are added to a serum containing only amboceptor they absorb the amboceptor and retain it firmly. Such cells are said to have been *sensitized*. If complement is added to sensitized cells they promptly dissolve. The substances employed in producing antibodies are called antigens.

Wassermann uses extracts of syphilitic tissues in the active stage of the disease for the antigen. The serum of known syphilitics inactivated at 56° C. is used as antibody. When these are mixed, the complement

is fixed and prevented from taking part in a subsequent hæmolytic reaction. When serum of unknown origin is mixed with extracts of syphilitic tissues and if the complement is fixed, it can be stated that the unknown serum contains the syphilitic antibody.

Noguchi simplified the technique for this test and his method is now in general use. The following apparatus will be needed: Several pipettes of 1 c.c. capacity graduated to 0.01 c.c, two 10 c.c. pipettes graduated to 0.1 c.c., several 1 c.c. pipettes graduated to 0.01 c.c., small test tubes, flasks as containers of physiological salt solution and thin glass tubing for making capillary pipettes.

The necessary reagents are as follows: The complement is obtained from the blood serum of guinea-pigs. The serum must be fresh and kept in the refrigerator. The amboceptor is prepared from the blood serum of rabbits which have been injected with human blood corpuscles.

The antigen is an alcoholic extract of certain tissues such as heart, liver or kidney. It makes little difference whether the extract is derived from syphilitic or non-syphilitic organs. A corpuscle suspension can be prepared with the blood of the patient being examined. The corpuscles are washed with normal saline solution by centrifugalization. The corpuscles are resuspended in normal salt solution, the standard amount for a test being 1 c.c. of a 1 per cent. solution of corpuscles.

To apply the test one drop from a capillary pipette (0.02 c.c.) of the serum to be tested is placed in each of two small test tubes. The tubes should be placed in two rows and two sets of controls should be made, one using positive syphilitic serum, the other normal serum. To each of these tubes add two units of fresh complement and 1 c.c. of the 1 per cent. corpuscle suspension. Antigen is added only to the tubes of the first row. The rack holding these pairs of tubes is placed in a thermostat or warm place with a temperature not over 37° C. for an hour. Two units of amboceptor are then added to all the tubes and the rack incubated at 37° C. for two hours longer.

If the reaction is positive there will be no hæmolysis in the tubes of the front row. The corpuscles settle at the bottom of the tube and the supernatant fluid is clear. The tubes of the back row and those of the negative control will all show hæmolysis.

The Butyric Acid Test.—Noguchi discovered that the syphilitic antibody is precipitated with the globulin of the blood serum or cerebrospinal fluid and that the globulin content of these fluids is increased in syphilis. This increase in the globulin is found earlier than the presence of the antibody and can be detected in the early stages of primary syphilis before the antibody. The antibody in cases of latent syphilis is apt to be inconstant while the increase in the globulin is nearly always

demonstrable. The cerebrospinal fluid can readily be obtained by lumbar puncture for this test.

The method of detecting an increase in the globulin content in the cerebrospinal fluid is extremely simple. Two parts of the fluid to be examined are mixed with five parts of a ten per cent butyric acid solution in physiological salt solution and the mixture boiled for a few minutes. One part of a normal sodic hydrate solution is then added and the whole boiled once more for a few seconds. The presence of an increased amount of globulin is indicated by the appearance of a granular or flocculant precipitate which gradually settles to the bottom of the test tube. Normal cerebrospinal fluid shows only a slight cloudiness and turbidity but no granular precipitate. The presence of blood in the cerebrospinal fluid renders the test valueless, so it is advisable when obtaining the spinal fluid to use two or three test tubes. The fluid to be used in the butyric acid test should be the last drawn.

The reaction appears more quickly and more distinctly the greater the amount of globulin present. Noguchi advises that the time period should not be greater than two hours before deciding whether the test is positive or negative.

He found the reaction appeared regularly in the cerebrospinal fluid of patients with syphilitic and parasyphilitic affections and also in all cases of meningitis from various causes. These acute inflammatory affections of the meninges are readily differentiated from syphilitic affections.

It is of the greatest prophylactic and therapeutic value to make the diagnosis of infantile syphilis as early as possible. If we knew that one of the parents of an apparently healthy newborn child was syphilitic, then we must observe the child carefully, so as not to overlook a possible specific infection. It must be remembered that infantile syphilis may run its course without any skin eruption, and may be recognized in practice only by a dry coryza, and a striking pallor, frequently combined with some enlargement of the liver and spleen.

Since, however, congenital syphilis is characterized in the great majority of cases by exanthemata, these must take a most prominent place in making a diagnosis. Since the individual skin lesions have been described before, it remains to discuss, at this point, the *differential diagnosis between the syphilitic and nonsyphilitic dermatoses of infancy.*

Syphilitic pemphigus neonatorum is distinguished from nonsyphilitic forms of pemphigus, aside from the predilection for the palms and soles, by its infiltrated base, and by the fact that the former is usually present at birth while the latter does not appear until a number of days after birth.

In distinguishing diffuse hereditary syphilitic skin infiltration in infancy from nonspecific diffuse inflammatory processes it is impor-

tant to remember that all erythematous lesions depending upon a mechanical, or chemical irritant show an intense, bright red color while that of the syphilitic dermatoses is a dull red with a brownish tint. The same difference is to be noted in making the differential diagnosis between syphilitic lesions and the diffuse reddening of the soles of the feet which is very frequent in atrophic infants and is dependent upon maceration. In the latter case, too, the characteristic induration and the later desquamation is absent.

With reference to the differential diagnosis between *eczema intertrigo* and diffuse syphilitic skin infiltration, the following points must be kept in mind:—The syphilitic skin lesion never causes such a brilliant, inflammatory, red color as the intertriginous eczema. Whenever and wherever present the former has always a suggestion of a copper red, or a yellowish brown color, that the latter never has at any stage. One can always tell upon careful examination by the stiffness of the tissues when we pick up an affected fold of skin, whether or not there is present a firm infiltrate as is the case in diffuse skin syphilis. In intertrigo, it will be remembered, there is active hyperæmia and swelling in the papillary layer and in the corium. These give the impression, however, to the palpating finger, of being soft and displaceable, and not of being a firm and unyielding infiltrate. The whole skin in the region of the nates and about the anus looks stiffer and smoother in the specific infiltration than in intertrigo, has a less brilliant color and does not have the swollen appearance of the intertriginous dermatitis. In the latter, too, especially in the genito-anal region one never sees at the height of the process any desquamation. Scaling could only occur when the acute inflammatory redness and swelling have gone down, *i.e.*, when the acute process has run its course and a restoration to the normal has nearly taken place. In diffuse skin syphilis of these regions, however, eroded and scaling areas may be situated side by side. It is a frequent occurrence to find the circumanal portion eroded but the skin of the nates themselves, dry, smooth, and scaling.

In the gluteal region of nonsyphilitic children, an exanthem composed of lenticular spots may occur, the individual lesions of which become eroded in a short time and very closely resemble moist syphilitic papules. These skin eruptions designated by Sevestre and Jacquet "syphiloides posterosives," are due to maceration and are distinguished from syphilitic papules by their brilliant inflammatory red color and by their isolated location on the nates and the posterior surfaces of the thighs.

The localization of the eruption is of value in the differential diagnosis of cutaneous syphilis of infancy. The efflorescence and infiltrations have a predilection for regions of the body that are exposed to chemical and mechanical irritations, therefore the lower half of the body and the face. The color of the skin is a further point in diagnosis. In

the majority of cases it is of a light gray, while the efflorescence itself is of a salmon, ham, or copper color. Only for a short time during the period of eruption is there a brighter red color.

The great value of enlargement of the spleen in the newborn and older infants has recently received renewed emphasis by Marfan as a point in the diagnosis of hereditary syphilis and is evident from the following figures established by Parrot:

Weight of spleen in children of 5 to 10 days	normal	7 grams.
	syphilitic	38 grams.
Weight of spleen in children of 10 to 20 days	normal	9.3 grams.
	syphilitic	34 grams.
Weight of spleen in children of 20 to 30 days	normal	8.3 grams.
	syphilitic	18 grams.

According to my observations, about 70 per cent. of all children that have palpable spleens during the first three months are syphilitic.

From the standpoint of differential diagnosis, several symptoms referable to individual organs should be mentioned. As far as the nose is concerned, there occurs in the newborn a condition in which the nasal mucous membrane becomes swollen, analogous to erythema neonatorum, and is accompanied by a slight snuffle, a condition that is physiological. There may occur likewise influenzal, diphtheritic, and gonorrhœal corzya of infancy.

The influenzal nasal affection which most frequently has to be considered in diagnosis, is always accompanied by catarrhal symptoms of the palate and pharynx that are absent in the syphilitic coryza. Congenital hypertrophy of the tonsils, too, can cause nasal obstruction in babies.

As to the mouth and pharynx, it must be remembered that in infants syphilitic efflorescences and ulcers are among the rarest lesions in these situations. By keeping in mind the peculiar butterfly shape of the ulcerations of the hard palate that are known as Bednar's aphthæ one will never confuse them with syphilis. The constantly changing epithelial defects of the geographical tongue (Landkartenzunge), likewise, have no resemblance to specific lesions.

The diagnosis of late hereditary syphilis must be made from the characteristic symptom-complex above described. The presence of a complete Hutchinson's triad, together with fixed pupils and radial scars on the lips, are weighty diagnostic criteria.

7. PROGNOSIS IN HEREDITARY SYPHILIS

In 18 families, with syphilitic parents, in which there were 161 pregnancies A. Fournier saw 137 still-births, *i.e.*, 85 per cent. J. N. Hyde found 916 deaths during the first year of life in 1121 syphilitic births.

Statistics from the Foundling Home in Moscow dating from about 1870 state that 70 per cent. out of 2038 syphilitic children died during their first six months of life. Fruhinsholz had 37 deaths among 84

congenitally syphilitic children (68.5 per cent., 29 of these deaths occurring during the first half year. Neither in private, nor in ambulatory clinical practice, however, does such a condition exist as these figures taken from institutions would indicate. Furthermore, the prognosis in children born with manifest syphilis, especially those born with pemphigus, is much more unfavorable than that of children in whom no evidence of syphilis is present till a later period. Such syphilitic children can be completely and permanently cured, according to our observations, so that they can be reinfected in later years.

Of the early manifestations of hereditary syphilis, the exanthemata and the osseous affections offer a good prognosis, except those in which pemphigus is present at birth, while visceral affections present at birth give a more unfavorable outlook.

Complicating affections and intercurrent diseases have a great influence upon the fate of these congenitally syphilitic children, especially during the first few months. Pulmonary affections deserve the first rank, and following them, gastro-intestinal diseases. Syphilitic recurrences exercise a peculiarly weakening influence upon the infantile organism during the first few months of life, because they very materially lower the resistance of the child to intercurrent diseases. It is impossible to decide definitely whether or not a peculiar predisposition for certain diseases exists in older children with syphilitic inheritance. The only causes of death that we have found noticeably frequent in these cases are pulmonary tuberculosis and tuberculous basilar meningitis, which must not be confused with syphilitic meningitis. The greatest factor in determining the later fate of these cases is whether or not an early and rational therapy was instituted in the individual case.

From my case histories I find that the patients who had no recurrences were almost invariably those that had been rigidly treated with mercury according to our directions for weeks and months. Although it cannot be denied that, in spite of careful treatment of the first period of eruption, recurrences are only too frequent, our experience teaches that in those children who were properly treated at an early stage, severe late manifestations in the form of destructive gummatous processes never occurred. Hutchinson's triad, too, does not occur under these circumstances.

On the whole then the bad prognosis given to congenital syphilis by obstetricians and syphilologists must be greatly modified and replaced by a more favorable one.

The early affections of the central nervous system, especially those classed as meta- and parasyphilitic, do not offer a good prognosis as to permanent cure; while the disturbances of locomotion due to bone lesions, as well as the early osseous manifestations, yield rapidly to rational treatment and are completely cured.

Recurrences of hereditary syphilis are much more frequent in untreated cases; 85 per cent. of all my cases of congenital syphilis of the fourth to the sixth month were cases that had not been treated before, and were brought for examination on account of a recurrence. The prognosis as to permanent cure in these cases is somewhat less favorable than in those cases that are properly treated from the start. Those that are not treated early are the ones, for the most part, that later give evidence of late hereditary syphilis.

What prognosis shall we give to cases of late hereditary syphilis? Skin and bone manifestations as such are doubtless curable in the majority of cases, and yet they are much more difficult to eradicate than those of early syphilis. In general, it may be said that those afflicted with such manifestations are to be considered below par with reference to their permanent state of health, and, in later life, they are candidates for parasyphilitic affections of the vascular and nervous systems.

Even more than in the case of the gummatous process of late hereditary syphilis the parasyphilitic affections of this period depend upon the treatment of the early manifestations of the disease. In my extensive material, tabes and paralysis occurred only in cases in which the early syphilis was inadequately treated.

ACQUIRED SYPHILIS OF CHILDHOOD

There is no essential difference between the acquired syphilis of the child and that of the adult. Well developed cases of acquired syphilis in children under observation from the beginning, show a primary lesion at the point of infection, which is followed after the proper interval by the development of indolent buboes and of a universal skin eruption. The majority of these cases, however, do not come under observation at the start, so that there is usually nothing left of the primary lesion. Moreover, the latter does not always appear as a characteristic Hunterian induration, but is frequently a simple papule. It is rare, too, that one sees the first exanthem. In our own ambulatory clinic these children with acquired syphilis present themselves as a rule with condylomata. Since the primary lesion and the skin eruptions are very frequently not well marked in children, they are apt to be overlooked, while the appearance of extensive condylomata causes the parents to seek medical aid. In localities where syphilis is endemic this is not the case, according to the reports of L. Glück of Sarajewo.

Contagion may take place in children just as in adults, *i.e.*, through venereal contact, through accidental transmission to the surface of the body, and through contact with unclean instruments in the hands of the physician. The following methods of infection must be considered as peculiar to children: (1) transmission at the time of birth from an actively syphilitic mother; (2) transmission through the act of

nursing; (3) transmission through various measures employed in the care of children.

A. Fournier denies the possibility of an intrapartum infection, believing in the validity of Profeta's law with reference to the immunity of a syphilitic mother. Nevertheless, six well authenticated cases of such infection have been described up to the present time.

Of greater importance is the possibility of infection through nursing. It is evident that a nurse with virulent syphilitic lesions on the breast can infect the child that nurses her. In that case a primary lesion forms on the lips, more rarely at the entrance to the nostrils. It is also conceivable that a nurse can transmit syphilis to a child, without herself being syphilitic if she nurses alternately at the same breast a syphilitic and a nonsyphilitic child. It has happened, for example, that the saliva of a syphilitic child served as the bearer of contagion to a well baby when the latter was given the same breast, without sufficient cleansing, immediately after the former had nursed. The presence of primary lesions simultaneously on the breast of the nurse and in the mouth of the baby can be explained only in this manner.

In those infections occurring as a result of the usual attentions given to infants and children, chance plays a prominent part. The primary lesion may be situated anywhere on the surface of the skin or mucous membranes. By far the most frequent seat in these cases is the mucous membrane of the lips, especially of the lower lip, because of the fact that feeding and caressing are the most prominent causes. Chancre of the eyelids, too, has been seen in children as a result of kissing.

The point of infection is only rarely the genitalia, and then much more frequently in girls than in boys. This method of contagion is sometimes the result of violence on the part of an individual who holds a view that is wide spread, that transmission of his disease to a young virgin will cure his own syphilis (A. Fournier). The finding of a primary lesion on the genitalia of a child should always be reported to the police, since it is probably the result of a criminal attack.

As to transmission by the physician in his professional capacity, this had to be considered formerly, as occurring through vaccination. Occasionally, ritualistic circumcision with accompanying sucking of the wound by the operator has led to infection in the child.

Our own experience and examination of the literature leads us to say that the site of the primary lesion is most frequently on the lips, less frequently on the face or neck, and still less frequently on the perineum, the abdomen and the genitalia. The least frequent of all in childhood is a chancre of the tonsil or of the tongue.

Chancre of the tonsil is, however, relatively more frequent in children than in adults, and is characterized by moderate enlargement of the tonsil together with ulceration of its surface accompanied by a

grayish, moist coating that has often led to a diagnosis of diphtheria. The submaxillary and cervical lymph-nodes are always enlarged, always bilaterally, though the chancre is of one tonsil only.

The course of acquired syphilis in childhood is generally a mild one, even in infancy. A. Fournier has reported cases of acquired syphilis in infancy, in which, on account of the enormous development of condylomata of the mucous membrane the nutrition was seriously impaired and a cachectic condition was produced. I myself have never seen such cases.

In older children, according to my experience, the first skin eruption causes no constitutional disturbances. I agree with Heubner who has called attention to the infrequency of a general eruption in acquired syphilis in children. Among 52 cases in my own material, both institutional and private, I could find a general eruption in only 13 cases, while all of the children showed at some time during the period they were under observation, moist condylomata in one location or another.

The exanthemata observed by me as the first in each case were invariably macular. Twice I saw an orbicular syphilide as an eruption occurring during a recurrence. In the case of endemic syphilis, according to the observations of Glück, somewhat different conditions prevail.

The great frequency of moist condylomata, with a predilection for the mouth and pharynx, the genitalia, the anus and the scrotum, is recognized by all (see Plate 25). Glück has frequently seen moist papules on the nasal mucous membrane as well.

The indolent polyadenitis of syphilis is always very well marked in acquired syphilis of childhood. The submaxillary nodes usually show the greatest enlargement even if there is no induration found on the lips, probably due to the great frequency of the primary infection of the lips in the form of a papule.

Heubner has pointed out the lack of resistance of these children with acquired syphilis to other infectious diseases. There seems also, according to my observations, a peculiar predisposition to later tuberculosis, much as is the case of children with hereditary syphilis.

Severe recurrences are less frequent in the acquired than in the hereditary form of syphilis, and the reappearances of the former are nearly always mild and yield most readily to proper treatment.

It is often necessary to make a differential diagnosis between hereditary and acquired syphilis in a child. The decision is often very important because the source of infection must be made out and removed. If we have to do with a hereditary transmission, then the diseased parent must be treated; if on the other hand the case is one of contact infection, then the bearer of infection must be discovered, eliminated from the household, and treated. If a primary sclerosis can be

demonstrated there is, manifestly, no doubt that the disease is of the acquired form; while diffuse infiltrations of the skin and mucous membranes, *i.e.*, diffuse palmar and plantar syphilide, infiltration and scars of the lips, diffuse rhinitis and nasal deformities during the first period of life, point unqualifiedly to hereditary syphilis. The differential diagnosis is generally more easily made during infancy than at a later period. The greatest difficulty arises in the case of children more than a year old with condylomata, because these can occur equally well as a recurrence of hereditary syphilis, or as a new manifestation of the acquired form. In many cases the history of the parent will disclose the hereditary nature of the disease. In dispensary cases such evidence is very frequently not obtainable; then the general condition of the child must decide. It is wholly improbable that a child with hereditary syphilis, untreated during the first year of life, is free from specific stigmata. These are usually abnormalities of the cranium and of the nasal skeleton as already mentioned. If these are absent and the general condition of the child is good, then one can diagnosticate acquired syphilis with certainty.

The presence of a syphilitic roseola on the trunk, speaks positively for the acquired type, as it never occurs there in the hereditary form. On the other hand, various disseminated exanthemata, such as the small papulæ and orbicular forms, may occur during the second year of life as manifestations of a recurrence of hereditary syphilis, although this is an extremely rare occurrence, and is never unaccompanied by other stigmata of the hereditary form of the disease, especially in the nervous system.

The differential diagnosis between late hereditary syphilis and the tertiary stage of acquired syphilis in children is much more difficult. *I know of but one pathognomonic symptom: the presence of radial scars on the lips. This occurs only in hereditary syphilis.* Hutchinson's triad is found also in tertiary acquired syphilis.

SYPHILIS AND INFANT FEEDING

It may be stated, first of all, that artificial feeding of congenitally syphilitic infants born at full term is attended by only slightly greater risk than in those that are free from this disease. In general, in order to avoid transmission to the person who nurses it, the infant should be artificially fed. Most authors, in deference to Colles' law, permit the mother who is free from syphilis to nurse her diseased child. The number of exceptions to this law have become so great, that Ogilvie, Finger, and myself, hold the view that infants with infectious lesions should not be permitted, off hand, to nurse their mothers. Since 75 per cent. of the exceptions to Colles' law were primiparæ, I might maintain that the latter should never be exposed to the danger of infection which nursing

carries with it; on the other hand, I have greater faith in Colles' immunity in the case of multiparæ and permit these to nurse their syphilitic babies.

What shall be done in the case of an actively syphilitic woman who gives birth to a healthy baby? Profeta's law claims immunity against specific infection for the offspring of a syphilitic woman, and Ehrlich's investigations show that the congenital immunity of the offspring of highly immunized animals, *i.e.*, mothers, is heightened by suckling the mother. The healthy child of a syphilitic mother has therefore only a very slight chance of becoming specifically infected during the first few months of life, even if it is nursed by its mother. A child that appears healthy at birth may therefore be permitted to nurse the syphilitic mother. The mother must be treated with mercury, and the greatest care must be exercised, as, for example, by permitting no caressing, so that the chances of transmission of the disease to the child will be reduced to a minimum.

The question will arise whether a child with syphilitic heredity shall be allowed to have a wet-nurse. The question may be considered under two conditions: (1) What shall be done if the child has symptoms of syphilis? (2) What shall be done in the case of infants that are born healthy, but have syphilitic parents?

In the former case the employment of a wet-nurse must be forbidden, even if after being fully informed of the nature of the disease and its contagiousness she is willing to nurse the baby. One would have to consider here not only the infection of the nurse, but also the possibility of a further spreading of the disease through her. The only condition under which it would be permissible to give the breast to a manifestly syphilitic newborn child would be that of producing a wet-nurse who had recently had syphilis.

In the second case, one can put a healthy newborn babe of a formerly syphilitic father to the breast of a wet-nurse without fear of contagion, but the child should be most carefully watched so that it can be taken from the breast at once and treated with mercury if it shows the first symptoms suspicious of the disease.

If unfortunately a wet-nurse becomes infected with syphilis from the child she is nursing, it is the duty of the family to have her undergo antisyphilitic treatment at once, and to safeguard others by preventing her from mingling freely with the outer world. She must either be kept isolated and treated in the household in which she became infected, in which case she may continue to nurse the child that infected her; or she must be treated in an institution and the child must be fed artificially. The former course is to be preferred.

It is self-evident that one must be mindful of the possibility of others in the household being infected by the syphilitic child, and

appropriate prophylactic measures must be taken. *The view that has been expressed many times that congenital syphilis is less contagious than the acquired form is erroneous.*

The possibility of infection of a healthy child through a wet-nurse who is syphilitic, either through previously acquired disease or through disease acquired in some manner during the nursing period, must still be considered. It is always a peculiarly embarrassing situation for the physician to find symptoms of syphilis in a wet-nurse employed for a child under his care. The nurse will always maintain that she was infected by the child, and this question must be settled first. From an examination of the child, or still more from the preceding observation of the child, it is usually not difficult to decide whether the child is syphilitic. The location and nature of the syphilitic manifestations in the nurse will, evidently, give valuable information as to whether the child was the source of her infection. One would be slow to accept the probability of transmission from the infant to the nurse, unless the latter had a chancre on the breast. The physician who examined the nurse before she was employed is very apt to be blamed for carelessness in his examination, although she may have been at that time in the first period of incubation, or in the latent period of a previously contracted disease, both of which conditions, of course, giving rise to no recognizable signs of the disease. In any event the nurse must be dismissed at once. If the child has not yet become infected, it will probably remain free from syphilis unless it is already in the incubation period. If it is infected or is in the period of incubation, then the removal of the nurse, who ought to be given thorough antisyphilitic treatment, will, at least, lower by one the number of carriers of infection in that particular family. The child taken from the breast of a syphilitic woman must under no circumstances be given to another woman to nurse, but must be fed artificially. If the child should not thrive on artificial feeding after a number of weeks, and still remains free from syphilis, then another nurse may be employed.

Antenatal Prophylaxis.—One should endeavor to prevent the birth of syphilitic children by appropriate treatment of the syphilitic parents, either before, or after marriage. Healthy children, further, must be protected against infection by a rigid surveillance of wet-nurses, and by all those measures that tend to prevent contact infection from one person to another. It is evident that a consideration of the "protection of the child against syphilis" should include also the "protection of the wet-nurse against syphilis from the child she nurses."

With reference to the prevention of syphilitic births, we should begin, first of all, with marriage. The important point here is to determine the state of health of the person who is about to marry. It devolves upon the family physician to insist upon a frank confession on

the part of the candidate for matrimony as to whether he has had syphilis, at what time, and with what symptoms, and not to permit marriage until at least four years have elapsed since the primary infection, during three years of which he has been treated systematically, and during the last six months, at least, of this time he should have been wholly free from symptoms of syphilis. Even with all of these precautions, too many syphilitic children will still be born to such parents. The only absolute protection against hereditary syphilis would be the prevention of the marriage of all men who have ever been syphilitic and their strict adherence to *coitus condomatus* in general.

In those rare cases where the woman was syphilitic before marriage, a much longer prohibition period should be enjoined, because the possibility of transmitting the disease to the offspring extends over a longer period of time in the case of the mother than of the father. Though it is permissible to allow marriage to the syphilitic if there has been a rigid enforcement of the above-named conditions, one should not encourage it.

Different conditions are presented to the physician if marriage has already taken place with one of the contracting parties syphilitic. If the man is in a period of latency, the woman free from syphilis, and the offspring nevertheless syphilitic, no matter whether born as the result of abortion, as still-births, or as manifestly syphilitic infants, the husband should undergo energetic treatment, to prevent the birth of other infected children. I do not consider it necessary to treat the mother in whom the physician has never seen evidence of syphilis, in the above circumstances, and I forbid the husband to have any intercourse with his wife during the period of treatment with mercury. If the wife becomes pregnant after the husband has completed this energetic treatment with mercury, it is still a matter of dispute whether she, too, should be required to take a like treatment. Those who believe that syphilis can be transmitted only by the mother, would treat the pregnant wife even if she had never had symptoms of the disease (Matzenauer, Mracek); I consider such a course superfluous. If, however, the pregnant woman had shown symptoms of specific infection either before or during her pregnancy, or if there is evidence of such infection from the history, then she must be given a most energetic mercurial treatment. Riehl has recommended for this purpose combining the constitutional treatment of the mother during pregnancy with the local use of vaginal suppositories each containing mercurial ointment 1.0 Gm. (15 gr.), cocoa butter 1.0–2.0 Gm. (15–30 gr.), a procedure that has the warmest approval of Vörner.

If the date of primary infection of the husband is far removed and the wife, who has remained and is now free from syphilis, becomes pregnant, it is advisable to omit all antisyphilitic treatment of both parties and quietly await the termination of pregnancy.

TREATMENT OF SYPHILIS IN CHILDHOOD

1. Treatment of Early Hereditary Syphilis.—Shall every child of syphilitic parentage be treated, no matter whether it has symptoms of syphilis or not, at birth? I would answer this question by saying that only those should be treated that have evident syphilitic symptoms, among which are to be classed not only skin affections, but also diseases of the nose, of the bones and of the viscera. A. Fournier holds the view that the healthy child of a recently syphilitic mother should certainly be treated, but that the healthy child of a mother with an older specific infection need not be treated. *I recognize but one indication for antisyphilitic treatment in the newborn and young infant, i.e., manifest syphilis, no matter whence it comes.*

The only effective therapy of early hereditary syphilis is administration of the preparations of mercury. In the front rank should be placed the internal use of the yellow iodide of mercury (protiodide), introduced as a therapeutic agent in infantile syphilis by Förster and L. M. Politzer, and now used exclusively at my clinic. We prescribe:

Protiod. hydrarg.	0.1	grs. iss
Pulv. acaciæ.	5.00	ʒi, grs. xv

divided into 10-15 powders, stirred in milk, and give to children 3 such powders a day, until all symptoms of syphilis have disappeared; after this we continue 2 powders for two weeks and then one powder for the same length of time. If extensive crusty and moist skin lesions are present, we use in addition baths of bichloride of mercury 1 Gm. (15 gr.) to 20 litres (5 gallons) of water and leave the child in this for 15 to 20 minutes.

Other preparations of mercury are calomel, hydrarg. tannic. oxydul., or a preparation much used in England, hydrargyrum cum creta (gray powder), all of which, however, are not to be compared with the protiodide in their effectiveness aganist syphilis.

French physicians, as for example at the Clinique Tarnier, use very extensively, the so-called *liquor van Swieten*, made as follows:

Hydrarg. chlor. corrosiv.	1.0	gr. xv
Alcohol	100.0	ʒ iii
Aqua dest.	900.0	ʒ xxx

10–30 gtt. per day.

The use of this preparation is all the more unjustifiable, in that it contains 10 per cent. alcohol.

Mercurial inunctions, too, are frequently used in treating syphilis in infancy. We have almost wholly abandoned its use during the first few months, as has also Finkelstein, but use it in preference to other preparations in syphilitic recurrences during the second and third years, especially in affections of the central nervous system. For inunction we may use the mercurial ointment, 10 per cent. colloidal mercury,

mercury resorbin, or mercury vasogen. One gram of the ointment is rubbed in daily for 5 minutes. The skin that is to be rubbed should first be washed with warm water and soap, and after the rubbing it is to be covered with a layer of absorbent gauze. In order to avoid irritation, a new area of skin must be chosen each day for the inunction.

The following arrangement for 10 days is a good one for children:

First day, left side of chest.	Sixth day, inner surface of left thigh.
Second day, right side of chest.	Seventh day, right calf.
Third day, left side of abdomen.	Eighth day, left calf.
Fourth day, right side of abdomen.	Ninth day, right arm.
Fifth day, inner surface of right thigh.	Tenth day, left arm.

The presence of bullous and crusty skin lesions, as well as bone affections contraindicates the use of the inunctions.

Subcutaneous injection of soluble mercury preparations offers no advantage over the other methods. The intravenous injection of soluble mercurial salts is still less to be recommended. The method introduced by Welander of using a little bag and the *merkolintschurz* of Blaschko patterned after it, I have abandoned as less efficient than other methods. The application of large pieces of various mercurial plasters to the back, as recommended by Unna and E. Lang, is a very effective method, but is apt to produce an undesirable skin irritation.

Since there is more at stake in the treatment of hereditary syphilis than of the acquired form, as the former is usually a matter of life and death, it is desirable to use only one method of treatment which we know will produce the desired result without causing other disturbances. From this standpoint I can recommend only the internal administration of the protiodide, and the inunction method, under the conditions described. The protiodide is especially well borne by the gastro-intestinal tract of children and only very exceptionally causes transient diarrhœa. *I have, myself, never had occasion to stop, nor interrupt, the treatment with protiodide.*

A really effective treatment of the child by means of the administration of mercury to the nursing mother is inconceivable, especially since the latest investigations of Somma have shown that mercury is not excreted with the milk.

The child requires no special care of the mouth during treatment with mercury, as the adult does. Salivation never occurs, to say nothing of mercurial stomatitis. The administration of mercury not only rapidly drives away all symptoms of syphilis in those infants, but likewise raises, noticeably, the hæmoglobin content of the blood.

The iodides are useless in the treatment of infantile syphilis. In syphilitic recurrence in the second or third year in the form of affections of the central nervous system and of the bones the iodides can be used internally as an aid to the use of mercury by inunction. About 0.3–0.5

Gm. (4½–7½ gr.) of sodium iodide should be given daily. The subcutaneous and intramuscular injections of iodipin can be dispensed with entirely. The treatment of individual important local affections must not be neglected.

Treatment of Rhinitis.—Local treatment is demanded if there is considerable nasal obstruction and much secretion. I have had the most satisfactory results with cotton tampons attached to a string, painted over with a 5 per cent. red precipitate ointment. Such tampons are placed alternately in one nostril and then the other, being left for one hour at a time. The nostril is first cleansed each time, with a moist cotton swab. Excoriations in the vicinity of the nostrils are powdered with the following:

℞ Calomel ..... 5..... ʒiss
Zinci oxidi ..... 5..... ʒiss
Amyli..... 50..... ʒx

If the nose is so obstructed that breathing and nursing are interfered with, it is well to put several drops of a 1–5000 adrenalin solution, in weak boric acid, into the nostrils a number of times a day. If there is a profuse purulent secretion, an effective remedy is found in the instillation into the nostrils of 10 per cent. perhydrol (*Merck*) or painting with 2 per cent. creosote glycerin.

Treatment of the Skin Affections.—This differs in no way from the customary treatment of skin lesions in acquired syphilis. Moist condylomata in the genito-anal region are best dusted with calomel powder and then covered with a layer of absorbent gauze that has been dipped in 5 per cent. salt solution. After the new skin has formed, the hypertrophic papules are to be covered with emplastrum cinereum. Unna's mercury-guttapercha plaster mull, as made by Beiersdorf of Hamburg, is peculiarly adapted to the local treatment of syphilitic skin lesions in children. Encasing the end phalanges of the fingers, or toes, in paronychia, with this plaster, gives extraordinarily good results.

It is best not to give any local treatment for the crusty, wide-spread syphilide. The bichloride bath, as an addition to the internal treatment, is of great value in this condition.

Ulcerations are to be covered with sublimate gauze and then collemplastrum cinereum spread on this.

Diffuse Skin Infiltrations require no local treatment, but complicating skin inflammations do. Furuncles and abscesses must be opened as soon as possible, and erosions of the umbilicus must be treated properly, best by cauterization with silver nitrate. It is a general rule that collections of pus, wherever localized, must be removed without delay.

Treatment of the Lesions of Mucous Membranes.—Since we have discussed nasal affections, and since other lesions of the mucous membranes are very rare in early hereditary syphilis, there is not much

more to be said here. Affections of the mouth and pharynx require painting with a 1 per cent. solution of bichloride of mercury, or a 10 per cent. silver nitrate solution. Local treatment of the laryngeal affections is impossible in early childhood.

Treatment of Bone Lesions.—Local treatment is not necessary. The bone swellings and the accompanying disturbances of motion are among the most satisfactory lesions in hereditary syphilis from a therapeutic standpoint. Phalangitis alone reacts a little less rapidly to the administration of mercury than do the corresponding early lesions of the long bones.

2. **Treatment of Recurrences of Hereditary Syphilis During Early Childhood.**—The use of inunctions is here the treatment preferred. This should be continued at least till all symptoms have disappeared no matter whether the syphilitic manifestations are of a gummatous of or a condylomatous nature. It is a good plan not to stop the inunctions at once after cessation of all symptoms but to follow them by a course of internal administration of the protiodide, giving 2 cg. ($\frac{1}{3}$ gr.) a day for two or three weeks. On account of the greater tendency to condylomatous and ulcerative affections of the mouth and pharynx, local treatment with such caustics as silver nitrate, bichloride of mercury, etc., is commonly needed. In affections of the central nervous system it is advisable to administer, simultaneously with the inunctions, sodium iodide internally 0.2–0.5 Gm. (3–7½ gr.) per day and to keep up the latter for from four to six weeks after cessation of all nervous symptoms. Isolated swellings of certain parts of bones call for the application of mercurial plaster in addition to the combined use of iodides and mercury.

3. **Treatment of Late Hereditary Syphilis.**—Here the iodides take first rank and nearly always bring about rapid improvement if only given in sufficiently large doses. The daily dose of the iodide salt, potassium or sodium iodide, is so regulated that the child receives a decigram (1½ gr.) per day for each year of its life. The iodide is prescribed in aqueous solution without syrup, and the appropriate dose is given three times a day in sweetened milk. Bardach recommends *iodferratose.* In case of severe visceral affections and in ulcerations, the iodide alone is sometimes inadequate and needs to be supported by a simultaneous treatment with inunctions of 2 to 3 Gm. (30–45 gr.), daily of mercurial ointment.

Marfan recommends here the subcutaneous injection of 5 c.c. of a 10 per cent. solution of mercuric cyanide every second day in combination with the internal treatment with iodide of potassium. In older children intragluteal injections of other soluble salts of mercury can be used, especially if it is desirable to get a rapid therapeutic action on account of the involvement of some important organ such as the eye or ear.

In general there is no difference between the treatment of late hereditary syphilis and that of the tertiary stage of acquired syphilis. It is even more important, however, in the former to look carefully after the general health and strength of these children who are nearly always cachectic. Following the specific treatment the use of remedies containing arsenic is to be recommended, such as Fowler's solution, Roncegno, Levigo or Guber water. If circumstances permit, drinking and bathing in the water of springs that contain iodide and arsenic are to be recommended.

4. **Treatment of Acquired Syphilis in Childhood.**—This is in every respect the same as in the adult; especially is this true with reference to the treatment of the primary lesion and the condylomata. The constitutional treatment should not be begun until the secondary manifestations have set in; then it should be pushed energetically and whenever possible in the form of inunctions. In older children, the mouth requires exactly the same care as that of adults who are taking mercury. I do not think it necessary to carry out the prolonged intermittent treatment in the acquired syphilis of childhood that is so much favored at the present time in the treatment of the adult, because of the relatively easy course and mild character of contact syphilis in childhood. I recommend treatment by inunctions until all secondary symptoms have disappeared, this treatment to be repeated as often as there recur any manifestations of the disease. One should make it a rule, to treat all recurrences of syphilis on the skin and mucous membranes, not merely locally, but also constitutionally, that is, with mercury in case of condylomata, and with iodides in case of gummata.

TUBERCULOSIS

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I. GENERAL OUTLINE

Definition.—Tuberculosis is an infectious disease which runs an acute, subacute, or even a markedly chronic course. Occasionally death supervenes merely days or weeks after infection, accompanied by astoundingly severe manifestations; in other cases the disease drags along for months, years, or even decades, and finally, after long and tedious suffering, results in a general disintegration; in yet other cases, the human organism may conquer and effect a cure. Tuberculosis may be localized in the various organs, or may be rapidly diffused throughout the body. Its clinical pictures are manifold, its anatomical aspects varying, its portals of entry diverse. The common factor, which unites all these different manifestations which we group under the general title of tuberculosis, is the causative agent: the tubercle bacillus. The definition of tuberculosis is therefore an etiological one, in contradistinction to the anatomical significance of the word tubercle, namely a nodule. It includes all those changes and conditions which are caused by the tubercle bacillus.

Etiology.—In 1882 Robert Koch discovered the tubercle bacillus to be the cause of tuberculosis, and thus segregated it as a *specific* disease, and enabled the varying clinical pictures (miliary tuberculosis, gelatinous tuberculous pneumonia, tabes mesenterica, acute hydrocephalus, etc.) to be united into the *etiological group* of tuberculosis. The infectiousness of tuberculous processes was previously known (Villemin, Cohnheim, and others) although disputed over and over. Koch's article dispelled all doubts. The tubercle bacillus is a rod 1.5–4 μ long, 0.2–0.4 μ broad, slightly curved, classified by Lehmann as a mycobacterium under the hyphomycetes. It grows slowly when cultivated, is immobile, and possesses a peculiar characteristic in being stained. It cannot be decolorized by acids after having been deeply stained by means of a dye and a mordant. Following such a procedure (see page 600) it appears coarsely granular (Fig. 137). Sunlight kills the bacillus quickly; intense diffuse light less quickly.

Whereas Koch originally considered the human and bovine bacil-

lus as identical, in 1901 he changed this view and declared them to be different. First, because animal experimentation showed that cattle injected or fed with pure cultures of human tubercle do not develop general tuberculosis; secondly, because man, in spite of his consumption of the milk or flesh of tuberculous animals, rarely develops primary intestinal tuberculosis. The investigations of P. and E. Biedert and of Ganghofner coincide with this new view of Koch's. [In 1896 Theobald Smith showed the non-identity of the human and bovine tubercle bacillus.] They showed that the morbidity of tuberculosis in man and in cattle by no means run parallel, that on the contrary, where tuberculosis is widespread among cattle the mortality of this disease is comparatively low and vice versa. Koch's view as to the difference of species between the human and bovine bacillus has been actively denied by other authors (Johne, Arloing, and others). However at the present time the discussion revolves more about the point as to whether we are dealing with two *species, different and totally separate,* or with one species descended from a common ancestor, which has gradually accommodated itself to its host and to its particular parasitic life, and thus in the course of time has developed two different varieties (Baumgarten).

The Imperial Health Department in an article by Kossel and Weber has made the following pronouncement:—Among the bacilli of mammalian tuberculosis, two types may be distinguished, which are best designated as the human and the bovine types. These two types show characteristic differences as regards their morphology, cultural aspects, and virulence for rabbits and cattle. A metamorphosis of the human type into the bovine type as the result of experiments on rabbits, goats, and cattle was not observed. By means of the bacillus of the human type a progressive tuberculosis in cattle could not be produced. In tuberculous individuals the bovine type is found relatively seldom, and as yet only *in children under eight years of age.* The tuberculous individual is a source of danger for cattle only in the rare instance of his excreting bacilli of the bovine type. On the other hand, the human organism seems to be capable of receiving the bovine type of bacillus. *Therefore the consumption of meat of tuberculous animals containing living bacilli of the bovine type, cannot be looked upon as insignificant for man. Especially is this true during childhood.*

The tubercle bacillus—we speak of the human type in particular—is very widely distributed, although not so nearly ubiquitous as formerly considered. Wherever the tuberculous individual goes, provided his excretions and secretions contain bacilli, there exists the possibility of dissemination. The vehicle of infection exists not alone in the sputum, but also in the finest particles of moisture expelled in the act of speaking, sneezing, etc. These become dry, and are later

raised with the dust. In the open air this is of little consequence, as the sun and even diffused daylight serve as most excellent disinfectants. It is, however, in the rooms and in the thickly populated dwellings of the poor, where sunlight and air do not enter or find their way but meagerly, that opportunity is offered for the increase of the masses of virulent bacilli. The bacillus of the bovine type is found more especially in the cow stalls, in all the excretions and secretions of tuberculous animals, as well as in their flesh and blood. It is found particularly in the milk of tuberculous cows, even in those not suffering from tuberculosis of the udder, and in the products of raw milk, such as cream, butter, cheese, curds, etc. Thus we see that all of us are brought into close relation with the bacillus and are in this manner exposed to infection.

Pathogenesis.—We must mention the paths, especially in childhood, by which the tubercle bacillus is able to enter the human body and produce tuberculosis. This question is by no means settled, but we shall attempt to discuss the contradictory views impartially, and to give the pros and cons of all sides. But let it be understood from the outset that no one claims that there is but one mode of infection by tuberculosis.

Innumerable opportunities for entrance are offered the tubercle bacillus, and at one time or another it may gain admittance anywhere in the body. Indeed the bacilli may even pass through the intact skin, if they are briskly rubbed over it; far easier, however, does infection follow if there is an injury to the cutis, whether it is caused by a tuberculous object, or whether the infection is added later. Marked examples of this class of cases are the local lesions that follow the handling of cadavers. I observed a case where a tuberculous mother, fearing tuberculosis following vaccination of her child, sucked the wound, and thus produced a localized tuberculosis of the skin. *In short, the tubercle bacillus may enter the human body at any point.* For us, however, the important questions are: Where does it enter in the majority of the cases? Where are the loci minoris resistentiæ? Where must we in general expect tuberculous infection?

There are three different views upon this subject, each of which explains the most frequent mode of infection in a different way:—(1) *by heredity of tuberculosis (prenatal infection)*; (2) *infection through the air-passages (aërogenic infection)*; (3) *infection through the digestive tract (enterogenic, or better, alimentary infection)*.

1. THE HEREDITY OF TUBERCULOSIS

Direct heredity of tuberculosis may be explained in two ways. Either the disease may be present in its true form at birth or in the fœtus (congenital tuberculosis), or the bacilli may be carried from the

parents to the offspring and remain temporarily latent, only to show their blighting influence when an opportunity presents itself (hereditary tuberculosis). In either case there is a real transmission of the bacilli in one form or another, and not merely the inheritance of a predisposition, a certain increased susceptibility to tuberculosis, which sooner or later may lead to disease. We shall later return to the question of predisposition.

The possibility of infection of the fœtus with tuberculosis is quite certain. There are a number of cases both in human beings and in animals which are unquestionable and therefore establish the fact without doubt.

The number of such cases considered reliable and unimpeachable varies according to the degree of scepticism with which one approaches the subject.

About twenty cases in man and some hundreds in cattle are substantiated in every particular. Huss accepts 40 human and about 100 bovine cases. Thieme examined the fœtuses of 86 tuberculous cows and found 2 tubercular. In one case the placenta was also examined and showed tuberculous changes. Klepp found among 4068 newborn calves 0.64 per cent. suffering from congenital tuberculosis, and in another series, among 847 calves, 1.18 per cent. Trustworthy reports of congenital tuberculosis in calves are frequently recorded; among such are those of Johne in 1885, Nocard in 1896, etc.

As a type of a convincing case in human pathology I shall cite that of Lehmann:

Woman, 40 years of age, in the ninth month of pregnancy, having suffered from tuberculosis for a long period, died three days after delivery. Autopsy showed old pulmonary tuberculosis, miliary tubercles throughout both lungs, scattered omental tubercles, tuberculous meningitis. Peritoneum and uterus, including placental surface, free from macroscopic tuberculosis. The child died 24 hours after birth. Autopsy showed aortic lymph-nodes the size of a pea or bean, hard, yellow, cut surface, granular. The bronchial lymph-nodes were still larger and appeared as a mass the size of a cherry, with cut surface as above. The lungs contained submiliary nodules, some as large as the head of a pin. Liver, spleen, and kidneys showed miliary tuberculosis. The nodules of all these organs proved to be tubercles of varying age, containing numerous bacilli. The age of the tubercles, according to the microscopic picture must be judged to have been over a week; the lymph-node tuberculosis of far longer standing.

However, although we must recognize the possibility of hereditary tuberculosis in man, it must be looked upon as very rare. Berend inoculated with tuberculin four children of tuberculous mothers and many born of healthy mothers, but did not obtain a positive reac-

tion in a single case. I myself attempted to diagnose tuberculosis in early infancy by means of tuberculin, but in more than 200 cases did not meet with a case of congenital tuberculosis, in spite of the fact that I gave especial attention to children of tuberculous mothers, in whom the clinical diagnosis had been substantiated by means of the tuberculin test.

The question of hereditary tuberculosis is far more difficult to settle. Not that there can be any doubt that it does exist, but because it is not easy to estimate the importance of heredity in the etiology of the disease. *Hereditary tuberculosis, i.e., the passage of living and virulent tubercle bacilli from the mother to the offspring certainly occurs.*

The first proof of the passage of tubercle bacilli from the maternal blood into the fœtal placenta and into the fœtal liver was offered by Birch-Hirschfeld and Schmorl. They performed a Cæsarean section post mortem upon a woman who died of miliary tuberculosis and removed the child who had died just previous to its mother. Since then, many cases have been reported, among which are some certainly open to question, as to whether hereditary or congenital tuberculosis existed. In such cases, a few days or weeks after birth, an advanced tuberculosis was found.

Bugge's case may be considered one of strictly hereditary tuberculosis: A woman, 39 years old, suffering from tuberculosis for two years, died four hours post partum, and her child 26 hours later. Tubercle bacilli were found in the blood of the child's umbilical vein and in a section of an hepatic blood vessel. Three guinea-pigs were inoculated with the blood from the umbilical vein, and a bit of lung and of hepatic tissue were inoculated subcutaneously. All three animals died of inoculation tuberculosis; no tuberculous lesions were found.

If we are to consider hereditary tuberculosis merely as a rare phenomenon, of little importance in the genesis of the great white plague, then we must give attention to another possibility. Our attention must be directed not alone to those few cases in which tuberculosis has been engrafted previous to birth, and which develop the disease in the first weeks or months of life, but we must presuppose that the *development of tuberculosis* may follow after a longer interval.

According to this view, the tubercle bacillus is transmitted far more frequently to the offspring, but lies dormant in the tissues of the child, and for the time being does no harm. Through one circumstance or another, such as an unfavorable mode of life, symbiosis with other disease germs, as, for example, with that of measles, a stimulus and impulse is given to the development of the bacillus, and, in that way, to the outbreak of tuberculosis.

We would thus have to distinguish between the infection of hereditary origin, and the evolution of the disease, which developed weeks,

months, years, even decades later, from the seed sown previous to birth. We would have to attribute to the tubercle bacillus the proptery of *latency*, the property of being able to exist permanently in its usual form, or we must say, that it may live in the tissues, capable of development but in a form not yet known to us (larval stage, Baumgarten).

As is well known, Behring, the exponent of the idea of infection during the first few days of extra-uterine life, believes in the longevity of the tubercle bacillus. If this be our standpoint, if we accept the possibility of latency, then we can understand that the teaching of the hereditary character of tuberculosis is gaining more and more support. This view, following the discovery of the tubercle bacillus, was entirely lost sight of. Baumgarten alone persisted during all these years in his view that the bacillus was frequently transmitted to the offspring, and can witness with pleasure the gradual spread of his ideas (Baumgarten, Jahresbericht, 1898, vol. xii, p. 570). The entire teaching of the heredity of tuberculosis will always be coupled with the name of Baumgarten. If his view as to the larval stage of the bacillus be correct, then we need not wonder at the negative results of the tuberculin injection in the case of infants who have the germ of tuberculosis in their organism. For the reaction is not the result of a tuberculous infection; the rise in temperature depends rather upon the vital reaction of the bacilli as the result of the injection of tuberculin.

When we weigh the pros and cons of such a broad interpretation of the heredity of tuberculosis, we must consider in the first place the experience of veterinarians, who show that calves which are immediately removed from their tuberculous mothers and reared away from all source of contagion, remain healthy.

Human pathology offers analogous observations. My own experience would seem to point in the same direction. Immediately after birth, children were separated from their tuberculous mothers and have so far remained free from tuberculosis. On the other hand, I know of three cases where the children of tuberculous mothers were likewise carefully guarded and separated from other tuberculous infection, but in spite of this, and although they did not react to tuberculin in the first weeks of life, they developed tuberculosis with a positive tuberculin reaction later in life.

A classical experiment of this nature was reported by Epstein at the Meran meeting of German scientists. A child was separated from its tuberculous mother immediately after birth and reared in the foundling asylum with other children. Notwithstanding this, it died of tuberculosis during the first year of its life. On the other hand, the same author reported instances where immediate separation of the mother and the child was followed by absence of tuberculosis in the offspring.

As an argument against the heredity of tuberculosis, Heller reports an observation concerning some guinea-pigs at the pathological institute in Kiel.

The pigs are descended from a number of animals which were rendered tuberculous with bovine material 14 years ago. All the descendants, some thousands, have always been healthy and strong with the exception of two short periods, during which several animals died of tuberculosis. Heller believes this infection to have been due to poor hay, without however offering any proof of this fact. Considering the great rarity of spontaneous tuberculosis among guinea-pigs, we may interpret these observations in another way: the latent disease may have been transmitted to the descendants, only to become active at the advent of some exciting factor, such as poor fodder. Such analogies may readily be drawn from families descended from tuberculous ancestors where we find a sudden outbreak of tuberculosis in one or more members.

Two facts favor the *probability* that hereditary tuberculosis is by no means very rare. First, experiments which show how easily we can artificially infect the offspring (Friedmann); second, the recent observations of Schmorl and Geipel as to the relative frequency of placental tuberculosis.

Although a number of cases of tuberculosis—by no means an insignificant number—are of hereditary origin, nevertheless heredity is not to be regarded as the sole nor even most important cause of the fearful scourge. Nor is there an iron law that the offspring of tuberculous parents or of a tuberculous mother must develop tuberculosis. On the contrary, we see that one or another child is spared, whereas others become its victims. Such selection may be seen also in the transference of the disease among members of the same family. We can therefore formulate two conclusions: (1) tuberculosis may be, but is not necessarily, hereditary; (2) tuberculosis may be inherited but may also be acquired. As regards the mode of hereditary transmission, we have the following possibilities:

1. Germinal Transmission. The seed carries with it the germ of the disease: (*a*) from the father; (*b*) from the mother.

2. Placental transmission: (*a*) with tuberculosis of the placenta; (*b*) without tuberculosis of the placenta.

3. Transmission intra partum.

1. GERMINAL TRANSMISSION

The male as well as the female seed may be the source of heredity. As regards heredity from the male, the experiments of Friedmann have shed much light. He injected a solution containing tubercle bacilli into the vaginæ of guinea-pigs immediately after coitus, and killed

the pigs within a week. In all the embryos tubercle bacilli were found, intracellular and lying within the embryonal cell layer. The organs of the mothers were in every case healthy; no tubercle bacilli were found in the vaginal or uterine mucous membrane. As the semen of those suffering from genital tuberculosis is almost always infectious, and as we may find tubercle bacilli in the semen, even in the case of general tuberculosis, where the testicle and epididymis are not involved, the possibility of transmission from the father must be regarded as definitely established. Practically, it is of no importance whether the spermatozoon is diseased or whether it is healthy and merely carries a tubercle bacillus with it. Probably, it must be healthy in order that the development of a fœtus may be brought about. The possibility of germinal transmission from the mother is also presented when we consider that ovarian and genital tuberculosis is by no means rare.

2. PLACENTAL TRANSMISSION.

We have already considered the question of transmission of tuberculosis where there is specific disease of the placenta. But is it perhaps possible that bacilli may pass through the placenta without causing tuberculous lesions; at least there are experiments which would tend to prove this.

3. TRANSMISSION INTRA PARTUM

This is of no practical importance on account of the rarity of tuberculosis of the vagina and of the external genitals.

APPARENT TRANSMISSION (TRANSMISSION OF THE DISPOSITION)

Heredity of tuberculosis by means of the tubercle bacillus must be definitely distinguished from what is termed the predisposition to tuberculosis. By the latter is understood a condition of the tissues which favors a growth of the tubercle bacillus independent of its portal of entry. A body so predisposed may be likened to a field prepared for the growth of some special seed. The resistance which every healthy body offers to pathogenic microörganisms is, in such cases, specifically diminished towards the tubercle bacillus. That certain individuals are more susceptible to tuberculosis than others is a fact that was recognized even at the time when the theory of contagion held sole sway. Koch recognizes the importance of predisposition. Besides taking into consideration a strong family tendency to the disease, he believes that the element of time is important; that the same person is far more likely to acquire tuberculosis at periods when his power of resistance is diminished. Baumgarten, on the other hand, in consequence of the views stated above, gives little weight to individual predisposition. He believes that man has a superlative predis-

position to tuberculosis, and that therefore this is not capable of being increased in the case of any individual.

It has also been urged against the theory of predisposition that members of tuberculous families are more exposed to infection, and that they are therefore more frequently afflicted with tuberculosis. Moreover the offspring of such families without a doubt show a diminished resistance to all harmful influences; the children of sickly and weakened parents are below the average in development and vital power. Epstein has pointed out the low average weight of infants of tuberculous mothers. I believe that we can speak of *paratuberculous* manifestations in such children, following the analogy of the offspring of luetic parents. The offspring of tuberculous parents, without really having tuberculosis, at times show certain outward signs of malnutrition. To what extent we are dealing with specific tuberculous manifestations in such children we cannot at present say. Other chronic and wasting diseases, especially when combined with poverty, may produce similar symptoms in the offspring. On the other hand, we find many children whose development is excellent in spite of a tuberculous taint.

2. INFECTION DURING LIFE

We now come to the consideration of tuberculosis acquired during life and first of all to the so-called aërogenic infection. Until lately the opinion that the tubercle bacillus attacks the child through the respiratory tract was not only the accepted, but almost the uncontroverted view. In pediatric literature the cause of tuberculosis is always given as due to inhalation of the bacillus. Even for the infant this was supposed to hold good.

As a proof of this belief it was stated that in children the lungs and bronchial glands are the sites of most frequent invasion. This argument formerly seemed to me sufficient, and I too was of this opinion. Nor can it be gainsaid that tuberculosis may be acquired through the respiratory tract. For instance, if a mason should inhale an infected splinter of stone, he might develop an inhalation tuberculosis. Even in this case, however, we should rather expect a primary tuberculosis of the larynx or of the larger bronchi.

In childhood opportunity for inhalation of tubercle bacilli is especially afforded when the children live among tuberculous people. This condition is particularly dangerous when the child is able to crawl about on the floor.

But from the clinical standpoint the question at once presents itself why we so rarely find primary tuberculosis of the larynx or of the larger bronchi, conditions almost unknown in younger children. How is it that the inhaled bacilli do not lodge in these organs instead of penetrating to the remotest parts of the lungs and to the bronchial lymph-nodes?

I II III

Tuberculosis of the lungs. Martha G., 9 years old. The three pictures taken within five weeks before death.

Such scepticism may be answered by quoting the large number of experiments whereby tuberculosis of the lungs was produced by inhaling powdered tuberculous material. These experiments always gave positive results. But the possibility that the bacilli entered the intestinal tract as well as the inspiratory tract must be considered, and therefore the possibility that the infection was enterogenic in nature. We must uphold von Behring in his statement that such proofs of inhalation tuberculosis must be carefully and critically reviewed.

In spite of the fact that the basis for the theory of aërogenic infection was far from sound, this belief gained general credence. Behring's startling communication in 1903 served to make us reconsider, and again brought forward the question of the enterogenic origin of tuberculosis. Behring maintained that tuberculosis of the lungs attacks the babe in its cradle, but that the milk which the infant drinks is the chief source of danger.

Behring's views must not be interpreted to mean that infection is due solely to bovine bacilli, as he said even in his address at Cassel that the danger lay in milk which contains tubercle bacilli, irrespective as to whether the bacilli are of human or bovine origin. In a later article he emphasized this point and enlarged upon it, adding that bacilli which are transmitted from mouth to mouth in the act of kissing, or are inhaled with the dust of infected rooms, are all swept into the intestinal tract by the milk.

When these new views of Behring's were made known, the natural assumption was that following an enterogenic infection we should have to look for the primary focus in the intestinal tract and in its regional lymph-nodes. But in direct contradiction to this theory, all investigations report that primary intestinal or mesenteric lymph-node tuberculosis is an *exceptionally rare* occurrence, notwithstanding which Heller found primary tuberculosis in this region in 30.7 per cent. of his cases (140 autopsies on patients who died of diphtheria but showed some tuberculous lesion).

Three possibilities have been considered as regards the mode of intestinal infection: (1) that there develops a primary tuberculosis of the intestine which gives rise to involvement of the mesenteric lymph-nodes; (2) that the intestine becomes the seat of a nontuberculous infection and thus allows the passage of tubercle bacilli and other microörganisms through its walls; (3) that healthy intestines allow the passage of tubercle bacilli, more especially during childhood. Some facts add weight to this view.

If the infection follows according to the second and third methods, the primary focus is in the mesenteric lymph-nodes. This focus may be very small, not even macroscopic, and nevertheless form the starting point of a severe general tuberculosis. Indeed I have seen cases

where the microscopic examination or even animal inoculation of the lymph-nodes was necessary to show the presence of tuberculosis.

There is one more possibility and one which has received too little attention, namely, that the bacilli can pass not only the intestine but also the mesenteric lymph-nodes without causing any lesions. We must remember that during digestion a strong current flows from the lumen of the bowel, and thence, traversing the intestinal wall, enters and passes through the mesenteric lymph-nodes. It does not seem unlikely that the tubercle bacilli, attaching themselves to the fat globules, may pursue this same course through the distended lymph-spaces and obtain an entry into the thoracic duct, thence into the venous blood stream and right auricle. From here they are transported to the capillaries of the lungs where the blood stream is slower and then enter the lymphatics. They next find their way to the bronchial lymph-nodes, which become the primary seat of the disease. When the lymph-nodes cannot receive any more foreign material, dissemination takes place in the lungs. Animal experimentation shows that the injection of tubercle bacilli into the jugular vein leads to a tuberculosis of the bronchial lymph-nodes and lungs. Also, that after giving tuberculous food, the capillaries of the lungs are full of tubercle bacilli.

Two points must be especially considered. First that the digestive apparatus does not commence at the stomach, but at the lips; so that at any point of the intestinal tract, from mouth to anus, infection may occur. And also that there are certain points which are favorable portals of entry for the bacilli. In young children the mucous membrane of the mouth is a locus minoris resistentiæ (of course not on account of dentition) as are also the pharyngeal and faucial tonsils, which through their crypts afford an excellent resting place for the bacilli. Whereas the stomach and small intestine appear rarely to be the seats of attack of the tubercle bacillus, the large intestine is frequently invaded. We may add that all bacterial infections attack this section of the intestine more readily than any other.

The tubercle bacillus may enter any part of the intestinal tract. In fact, under certain conditions it may gain admittance to any other part of the surface of the body, whether it be covered with mucous membrane or skin. According to our present knowledge, we may say that any part of the human body may at some time serve as the portal of entry for the tubercle bacillus. But as to the question of the chief mode of infection, our knowledge is by no means precise. This being the case, we must not direct our efforts of prophylaxis to one point alone but must consider the manifold ways in which a child may be exposed to tuberculosis.

Pathological Anatomy.—The tubercle bacillus having gained entrance into the body in one way or another, three possibilities present

themselves. The organism may conquer the bacillus and thus prevent the development of disease. This happy event may be brought about by the lessened virulence or small quantity of the infecting microörganisms, or by the strong protective powers of the child.

Second, the bacilli may remain in the tissues without causing disease or increasing in number. After a long period such bacilli, becoming more virulent through weakening of the protective agencies of the body, or through a favorable symbiosis with some other germ, may increase in number and give rise to the dread disease.

The third possibility is that immediately, or soon after entry into the body, the bacilli bring about the anatomical changes constituting a primary tuberculous lesion.

The tubercle, which gives its name to the disease, is a circumscribed inflammatory growth. It may be so small as scarcely to be perceived with the naked eye, or it may grow to the size of a millet seed or a pea. Its color is grayish yellow. Histologically it consists of closely packed epithelial cells, among which may be found giant cells, especially toward its centre. The tubercle bacilli are either extracellular or intracellular. Characteristic of the tubercle is the lack of blood vessels. The tubercle is not caused by the vital activity of the bacillus, as dead bacilli or even foreign bodies may give rise to it. However, the further changes that the tubercle undergoes are due to the activity of the bacillus. They are the cause of the rapid central necrosis, the degeneration that transforms the nodule into a cheesy mass.

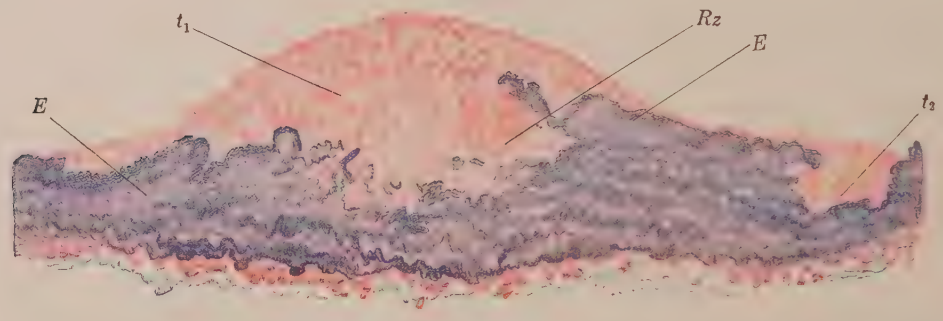
Besides the power of the tubercle bacilli to form tubercles and to cause cheesy degeneration, they are able to act as a true agent of inflammation and to cause exudative processes. It is true that this is exceptional, unless they have spread from their primary focus.

The spread of the germs may take place in many ways. In the majority of cases it occurs by *contiguity;* one tubercle forms next to the other, until they are all fused into a cheesy mass, forming the conglomerate or solitary tubercle. As an example of spread by *contiguity* we may cite tuberculosis of the intima of a vessel which, by contact, may form a tubercle on the intima of the opposite side (Fig. 136).

The second method of diffusion is by means of the body fluids, the secretions and the excretions. For example the urine may be the cause of development of tuberculosis of the bladder in a case of tuberculosis of the kidney. Or, again, one lymph-node may infect its neighbor, the bacilli being carried with the lymph-stream. Indeed, retrograde infection is conceivable in such a case if a node is so diseased that it offers a hindrance to the lymph-stream and causes stasis. In such a case, the bacilli would be carried against the lymph-current to lymph-nodes distally situated.

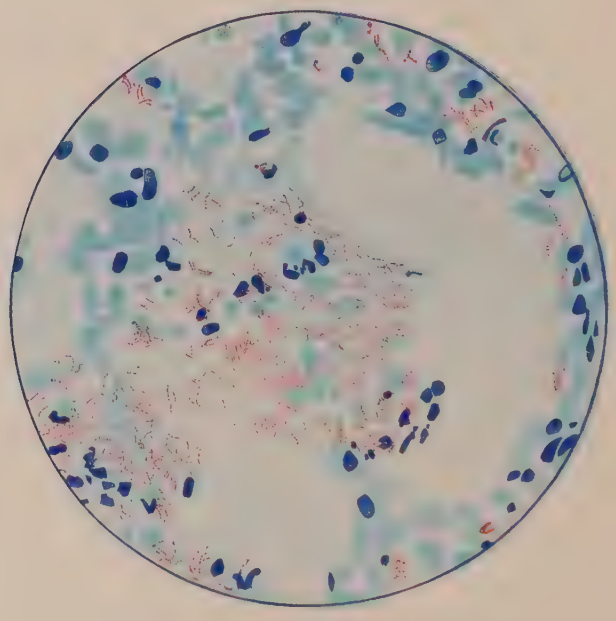
The third way in which tuberculosis may spread is by means of the blood. The bacilli may enter the blood in different ways: (1) the germs may at once enter the blood from the lymph and cause primary tuberculosis of the vessel wall. This may later give rise to a general miliary infec-

FIG. 136.



Tuberculosis of the intima of a pulmonary vein.—*t*, tubercle; *Rz*, wandering cells; *E*, elastica intima, in which the elastic fibres in the vicinity of the tubercle are completely destroyed; t_1 and t_2, tubercles in the vein.

FIG. 137.



Tubercle bacilli in the tissue of the lung.

tion; (2) a tubercle in the neighborhood of the vessel may undergo degeneration and rupture through the vessel wall; (3) bacilli may find their way from the lymph-stream into the thoracic duct and thence into the venous blood, finding their way into the lungs and arterial circulation.

In any of these three ways a general infection by tuberculosis may be brought about. However, in the case of tuberculosis by contiguity, and very often when the disease is spread by the excretions or secretions, it may remain localized to a single organ or confined to a system of the body.

The peculiarities in the pathology of the disease which childhood exhibits are: very rapid growth; early degeneration of the tubercle; typical formation of miliary tubercles with giant cells, especially associated with subacute miliary tuberculosis; frequent tuberculosis of the intima of the vessels; the predominance of gland, bone, joint, brain, and meningeal tuberculosis. Finally, and this is especially true of young children, the frequency of generalization, and the rarity of signs of reaction in the surrounding tissues, which indicates the slight tendency towards healing.

Frequency.—Tuberculosis is a very frequent disease of childhood. The importance of this fact becomes more evident the longer one studies the subject of tuberculosis in children. However, the statistical basis for such an opinion is indeed scanty and contradictory in many particulars. In Vienna, Hamburger and Sluka found tuberculous lesions in 40 per cent. of the cases, agreeing with the figures of Schmorl in Dresden. The following table which they give, shows the frequency of tuberculosis in relation to the various ages:

Age.	Number of Autopsies.	Non-Tuberculous.	Tuberculous.	Percentage of Tuberculous.
1	154	130	24	16
2	88	51	37	42
3 and 4	80	33	47	59
5 and 6	29	12	17	60
7–10	28	10	18	64
11–14	22	5	17	77
Total	401	241	160	40%

We may thus see that it is by no means rare to find tuberculosis in children, and that the nearer we approach puberty the oftener it is met with. The clinician must therefore look for tuberculosis in children of any age.

Diagnosis.—The diagnosis may be so evident that it can be made at a glance, or it may be attended with the greatest difficulties requiring the aid of all the resources at our command.

The *history* may give us an important clue. In every case we should learn whether either of the parents or grandparents had died of tuberculosis or hæmoptysis, or whether numerous members of the family died at an early age. Such inquiry may prove negative and nevertheless we may be dealing with a case of tuberculosis. It may even happen that tuberculosis in the child discloses the fact that the par-

ents were afflicted with the disease. I could cite numerous cases where after finding definite signs in the offspring, a careful examination for the first time disclosed tuberculosis in the mother and father. Furthermore we should enquire whether the child has come in contact with any one suffering from tuberculosis, even though it has been for

Fig. 138.

Advanced pulmonary tuberculosis. Enlarged glands in the neck.

Fig. 139.

Posterior view of same child, showing extreme emaciation.

only short periods (servants, midwives, teachers, etc.). Often tuberculosis is contracted from living with a tuberculous person for a short time, especially in the case of a child. Wassermann reports a case where an infant contracted a fatal infection as the result of living for only eight days with a person suffering from tuberculosis.

After the history has been taken, an *inspection* of the patient should aid us in the diagnosis. Not infrequently, especially in children near puberty, we meet with the typical phthisical habitus. The peculiar build and carriage recognized even by the laity, tells us that we are dealing with a tuberculous individual. These children are tall for their age, or at least appear to be, on account of the disproportion between the width of their chests and their height. The long and

FIG. 140.

Pulmonary tuberculosis in a thirteen-year-old girl.

FIG. 141.

The same case. Raising the arms shows the "phthisical habitus" more plainly.

thin extremities and scrawny necks enhance this effect. The fingers, too, are long and thin, the distal digits being thickened and club-shaped. The chest is flat, expanding feebly upon deep inspiration. The scapulæ are situated low and the shoulders converge anteriorly; the ribs stand out prominently (Figs. 138–141).

Although the picture is shocking when it presents itself in its most extreme form, it may be even attractive in the case of certain individuals. Artists have frequently pictured a beautiful type of con-

sumptive. Only recently, I saw a little girl (Plate 32) whose long eyelashes, bright eyes, wealth of hair, and sweet expression made her a picture of loveliness. The same plate shows the wasted figure of the child when seen unclothed, and gives a schematic drawing of the extent of the lesions which were found in the lungs. Children under ten years of age are more rarely of this type. But even very young persons may have the phthisical habitus. In them it generally presents itself as extreme emaciation. Further inspection may reveal bone or joint diseases, perhaps of the knee or hip, or we may notice a spina ventosa or involvement of the superficial lymph-nodes, especially of those cervical nodes which lie close to the lower jaw or in the supraclavicular region. Scars in this region may tell of lymph-nodes which have ruptured in this area.

The skin is often grayish yellow, discolored, and of striking dryness. Tuberculids, lupus, or peculiar furuncular lesions, which remain in a stationary state for weeks or months, or show no tendency to heal, have of late been frequently described as concomitant symptoms of a general tuberculosis. In young children a peculiar odor, the cause of which is not yet known, is frequently noticeable.

Palpation will disclose the lymph-nodes just mentioned. Their lack of tenderness speaks against simple inflammatory origin. The spleen is often much enlarged, especially in general tuberculosis, although it cannot be considered a pathological symptom.

The fever is in no way typical. It is rather dependent upon infection due to secondary microörganisms. There are indeed cases of tuberculosis in children which give rise to little or no fever.

Auscultation and percussion are of great diagnostic value in those cases of chronic illness where an infiltration of the lungs is present. In childhood, however, we do not find tuberculous infiltrations or tuberculous pneumonias which develop gradually and progress slowly.

Physical signs enable us to make the diagnosis of tuberculosis only when we find a cavity. Hæmoptysis, provided we are sure of its pulmonary origin, also allows of this diagnosis. The respiration in tuberculosis is by no means characteristic. The cough may at times be suggestive, for example, paroxysmal attacks point to tuberculosis of the bronchial lymph-nodes. It may, however, resemble in every respect the cough of other pulmonary affections. Examination of the urine does not supply any definite diagnostic criteria. Indicanuria points to tuberculosis, but its absence is not positive evidence against the presence of the disease. Convulsions, which in miliary tuberculosis usher in the end, and those focal symptoms which originate from solitary tubercles in the brain, are worthy of mention. Ophthalmoscopic examination of the fundi, in exceptional cases, shows the presence of chorioid tubercles early in the disease, and thus clinches the

diagnosis. [This examination is not infrequently of diagnostic value in the differentiation of cerebrospinal and tuberculous meningitis and should not be omitted in cases where the etiology is not clear.—A. F. H.]

Whereas the methods of examination which we have thus far mentioned afford us only exceptionally absolute proof of the nature of the disease, we must now consider two pathognomonic tests: first, the finding of the tubercle bacillus, and second, the injection of tuberculin.

Finding the tubercle bacillus in childhood is associated with far greater difficulties than in the case of adults; for, whereas the latter generally suffer from open tuberculosis, that is, from a form of the disease which communicates with the bronchi and upper air-passages children more often are affected with the closed variety. Furthermore, babies swallow their sputum. *However, under all circumstances where tuberculosis is suspected we should try to find the bacillus.* If no sputum can be obtained we may tickle the entrance of the larynx with a bit of cotton held by a forceps, in order in that way to excite an attack of coughing which may bring up some mucus; or we may introduce a catheter into the larynx and aspirate material for examination. Some have recommended washing out the stomach, especially early in the morning, in order to obtain bacilli which may have been swallowed in the course of the night. In the case of older children we may resort to Blume's method of having the child cough upon a glass slide, in order to obtain a few drops for microscopical examination.

If these methods fail, an examination of the stools for tubercle bacilli must be made; and if they are found, they cannot be considered due to an intestinal lesion. They may equally well have been swallowed and have their source in a tuberculosis of the tonsil or of the lungs. Strassburger's sedimentation method is used to detect the bacilli. This consists in mixing a small amount of stool with water, adding alcohol or alcohol and ether to the supernatant fluid, then allowing it to settle and examining the sediment for bacilli.

We must also not neglect to look for bacilli in the sediment of the urine. They may be found not only where tuberculosis of the genito-urinary tract exists but at times when the disease is located elsewhere.

Examination for tubercle bacilli in sputum, in the urinary sediment, in feces, and in the stomach contents is best carried out as follows:

1. Spread the material as thin as possible, allow it to dry, and fix by passing through the flame three times.

2. Stain for two minutes with carbolfuchsin, holding it over the flame until the solution begins to steam [fuchsin 1 Gm. dissolved in 10 c.c. of absolute alcohol, to which 100 c.c. of carbolic acid (5 per cent.) is added].

3. Wash with water.

4. Decolorize for about 30 seconds in a hydrochloric acid-alcohol mixture (10 c.c. conc. hydrochloric acid, 990 c.c. 70 per cent. alcohol).

5. Wash with 60 per cent. alcohol until all the red color is removed.

6. Counterstain with weak aqueous methylene blue solution for 1–2 minutes (1 c.c. conc. aqueous sol. of methylene blue to 10 c.c. of distilled water).

7. Wash and dry with filter paper.

If the excreta show no tubercle bacilli, we may resort to an examination of the blood. For this purpose, 1–2 c.c. of blood are obtained from the median vein and injected either intraperitoneally or, if we are anxious to know the result more quickly, into the mammary gland of a guinea-pig which is suckling its young. However, even if the blood contains bacilli, we shall probably not discover the fact until the patient has died. Nevertheless the method is of value to establish the diagnosis when we do not believe an autopsy will be granted.

Lumbar puncture may show the bacilli in miliary tuberculosis in spite of the absence of all clinical symptoms which might point to an involvement of the meninges.

If the find the bacillus in one or other of the above ways, the diagnosis is established. However, if we do not find it, as is so often the case in the early stages, we may resort to the second method, which consists in the *Diagnostic Injection of Tuberculin.*

Robert Koch discovered in 1890 the fact that certain constituents of the tubercle bacillus have the property of causing specific reactions in the tuberculous individual, when *subcutaneously* injected.

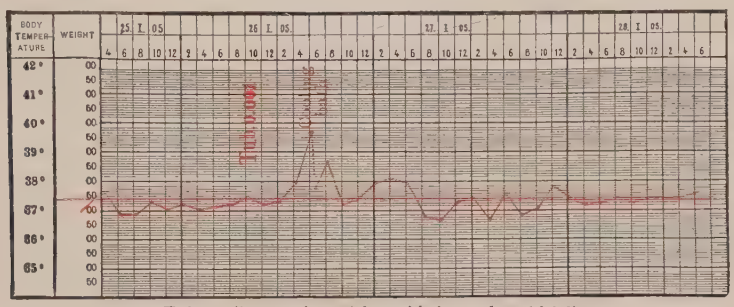
The agent used to establish this reaction he called tuberculin. At the present time it is often referred to as "old tuberculin." The official name is tuberculinum Kochi, and when the term tuberculin is used, it should be understood that it is this preparation that is referred to. It is a clear brown fluid which, in accordance with Koch's directions, is prepared from cultures of the tubercle bacillus in glycerin bouillon by filtering off the bacilli and compressing the filtrate into one-tenth of its volume. Its essential constituents are the soluble secretory products of the tubercle bacillus. In Germany the manufacture of the preparation is under State control, and 1 c.c. of it costs M. 1.50 (40 cents).

In order to obtain the reaction, tuberculinum Kochi is diluted with water without any antiseptic, and the best method is to prepare, under aseptic precautions, a solution of 1:100, which is again adequately diluted before injection. The mother solution of 1:100, if preserved in the dark and at a low temperature, will keep a few days. Caution, however, should still be exercised, as a slight turbidity will indicate that the preparation is no longer effective. The injection is made into the

subcutaneous cell tissue of the back or abdomen, the place of puncture having first been suitably prepared.

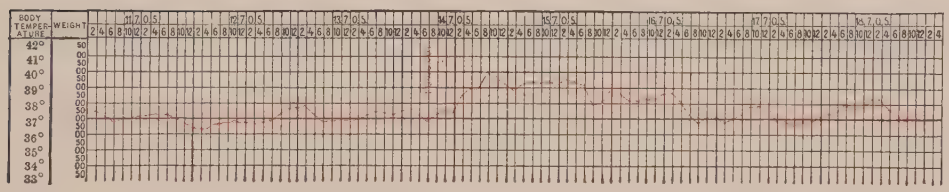
Prior to the test injection of tuberculin it is necessary to make sure of the afebrile condition of the subject. I always have the temperature taken twice during the twenty-four hours preceding the injection, and

FIG. 142.



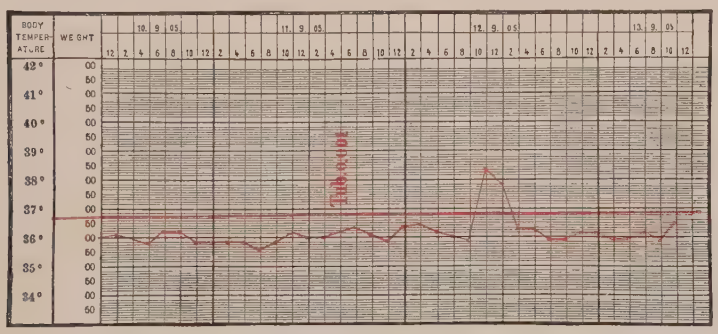
Tuberculin reaction with rapid rise and rapid fall.

FIG. 143.



Protracted tuberculin reaction.

FIG. 144.



Delayed tuberculin reaction.

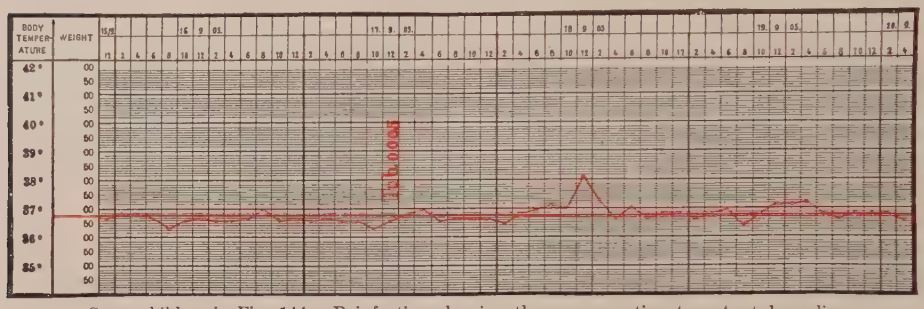
if the same should exceed 37.5° C. (99.5° F.), I absolutely decline to inject.

The *dose* depends upon the condition of the patient. The test injection should never be commenced with more than 0.001 gram and, as a rule, it is even better to reduce the same to $\frac{1}{2}$ or $\frac{1}{10}$ this quantity, thus commencing with 0.0001 gram. This holds especially good for all cases in which there are manifestations of pulmonary infiltration or there is

suspicion that the lungs are involved by the tuberculous process. In these cases the first test injection had better be reduced to 0.00001 gram, the injection repeated, and if this should be negative, the injections may be continued with five or tenfold doses, and so on.

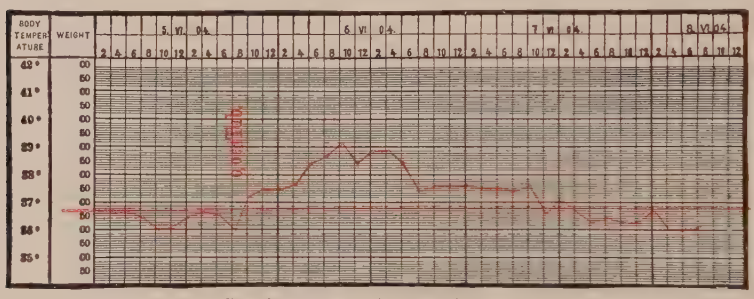
The tuberculous organism will react in a threefold way on the injected

Fig. 145.



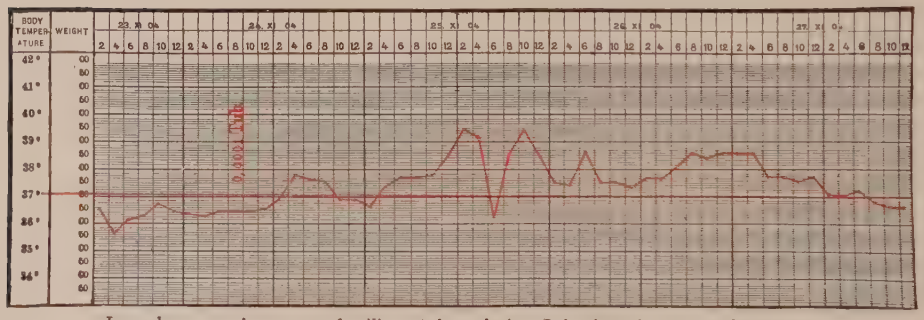
Same child as in Fig. 144. Reinfection showing the same reaction type to tuberculin.

Fig. 146.



Step-like ascent of tuberculin curve.

Fig. 147.



Irregular curve in a case of miliary tuberculosis. Injection given a week previous to death substantiated the diagnosis.

tuberculin. There will be (1) a general reaction, (2) a focal reaction in all tuberculously affected parts of the body and (3) a local reaction around the place of injection.

1. *General Reaction.*—Provided a minimal dose, suited to the individual case, has been administered, the temperature will first slowly rise in about four to six hours after the injection, then rapidly rise after a

further two to four hours. Then it will gradually decline and return to normal inside of twenty-four hours. In some cases the access of fever may last somewhat longer and exceed even twenty-four hours. It is said by some authors that the protracted reaction occurs oftener in children than in adults. In a third class of patients the rise in temperature will occur considerably later, or the elevation take place slowly. The fever period is sometimes associated with headache, general malaise, possibly reduced appetite, and occasionally vomiting. Generally speaking these subjective manifestations are much less severe in children than in adults. The younger the child is, the less will be the manifestations, and in most cases an increased demand for sleep will tide them over the period of reaction. Of course, it is necessary for children to stay in bed all the time.

The reaction is considered positive, if the rectal temperature rises above 37.6° C. (99.5° F.), or if it exceeds by more than 0.5° C. (0.9° F.) the previous determinations. If there is no reaction, or if the reaction leaves any doubt as to whether it is positive, the injections are repeated in slowly increasing doses and suitable intervals (twice or three times in twenty-four hours), until a dose of 0.01 gram will decide the question. I have never known the subcutaneous tuberculin reaction to fail with this method of procedure. When it was positive and I had an opportunity to follow the case up, or to witness the autopsy, the presence of tuberculosis was always reliably demonstrated. When it was negative, we have never found tuberculosis at autopsy. Of course, the reaction merely indicates a tuberculous involvement, and not the presence of a tuberculous infection. I have never observed any injurious effect upon injected children and am, therefore, unable to agree with the contrary opinion of other authors, such as Neumann for instance.

2. The *focal reaction* finds expression in increased blood supply to all specifically affected tuberculous parts of the body. Even when apparently healed, they will swell under the influence of the injected tuberculin, become hyperæmic and proliferate more vigorously; in short, all parts which have ever undergone anatomical changes of a tuberculous origin, and where there are still specific changes, will demonstrate reactive processes. Under certain circumstances the focal reaction may be of diagnostic importance inasmuch as it proves definite parts as tuberculously affected (articulations). Lastly, those parts of the skin where a cutaneous reaction had preceded the subcutaneous injection will again flare up.

3. *Local Reaction.*—There are two kinds of local reaction:

(*a*) Around the puncture of the needle which at the time of injection has penetrated through the epidermis into the tissues, there is often hyperæmia and swelling six to eight hours after injection. This may persist for several days and vary in diameter between 1 mm. and 1 cm.

This is the "puncture reaction," and I wish it to be distinctly understood that by puncture reaction I mean the manifestations just described, and no others.

(*b*) At the place where the point of the needle has introduced the tuberculin into the subcutaneous tissue there is another reaction, occurring a few hours after injection, which consists in swelling of the subcutaneous tissue, with possible tenderness on contact or pressure, and followed later by hyperæmia of the skin. It is opportune to thoroughly distinguish between the subcutaneous and puncture reactions. The places where they occur may be somewhat distant from each other if the needle has been pushed forward under the skin, driving the fluid for some distance into the subcutaneous tissue; in other cases the puncture reaction may, so to speak, form the centre of the subcutaneous reaction. The question whether a puncture reaction will occur or not depends upon the mere accident whether the epidermic layer has imbibed some of the tuberculin when the needle was inserted or withdrawn, whereas a distinctly visible subcutaneous reaction is rarely absent.

Local reactions have been described years ago by Epstein, Escherich and Schick, but in those early publications the difference between puncture and subcutaneous reactions has not been sufficiently emphasized and what is now known as "Depot" or subcutaneous reaction was included in the designation of puncture reaction. Latterly great value has been attached to the subcutaneous reaction by Hamburger as a decisive sign for the presence of tuberculosis.

The subcutaneous application of tuberculin for the purpose of establishing the diagnosis of tuberculosis is still to-day the subtlest and safest method. It is not applicable in febrile cases; it requires taking the temperature every two hours; rest in bed; nearly always clinical observation, and devolves a certain measure of inconvenience upon patient and attendant alike. Toward the end of life it may fail in individual cases. But these disadvantages are outweighed by the absolutely safe findings with correct procedure.

However, the tuberculin test had not met with general appreciation for diagnostic purposes until von Pirquet introduced, in 1907, its *cutaneous* application. This author explained the reaction in tuberculosis by assuming that the tuberculous individual is allergistic to tuberculin, which means that his reactive capacity is different from that of the healthy, or rather nontuberculous individual. This, for instance, is also exemplified by the fact that cutaneous inoculation of tuberculous subjects with tuberculin produces a focus of inflammation in the shape of a papule, measuring from 5 to 20 mm. in diameter. In his first experiments von Pirquet availed himself of a 25 per cent. tuberculin solution, but later he has decided to use undiluted tuberculin in all cases.

The technique in producing a cutaneous reaction (Pirquetisation)

is as follows: The part of the body where the reaction is intended to take place (upper arm, lower arm, lower part of the thorax) is cleansed. One droplet each of undiluted tuberculin is applied to two spots of the skin about 6 to 10 cm. apart. By means of a serviceable instrument, such as Pirquet's original instrument, an inoculating lancet, needle or something similar, the skin midway between the two droplets, or just above, is so lightly scratched that not a particle of blood may exude. This is done as a control. Next, with the same instrument, the same degree of energy, and in exactly the same way, the two places are inoculated, on which the two droplets of tuberculin had been deposited. The excess tuberculin is neatly removed with a cotton swab, care being taken that no part of the tuberculin may come in contact with the control scratch. This completes the inoculation. No bandage is necessary, but no harm is done by applying a cotton layer which should be fixed with adhesive plaster. It is advisable to use the set of instruments introduced by von Pirquet for two reasons: (1) By using the identical instrument in all cases, the reactions obtained will admit of comparison in regard to intensity, and (2) the skin may be easily scratched too deeply when a strange instrument is used. With Pirquet's instrument a very slight drilling motion is executed. Any hæmorrhage destroys the test.

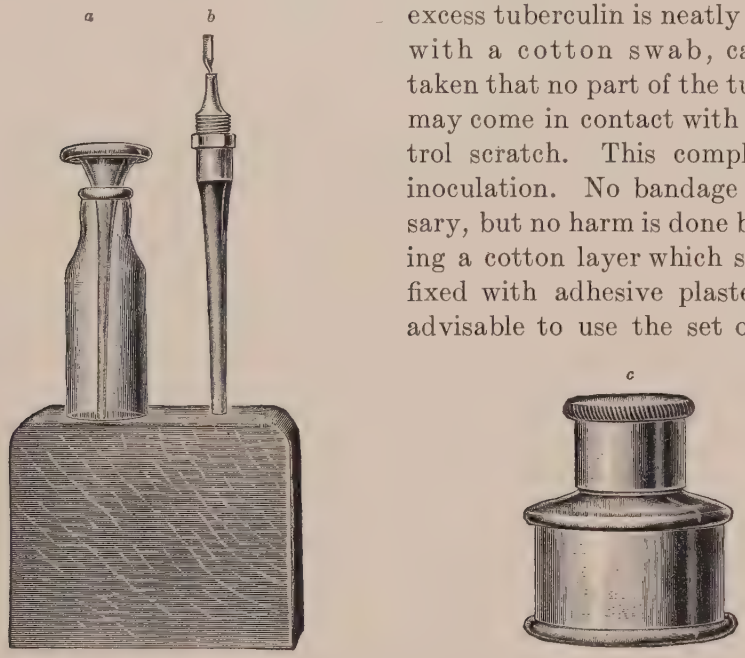


FIG. 148.—Set of von Pirquet's original instruments for cutaneous reaction. (*a*) Receptacle for the instrument, with glass stopper; (*b*) the actual instrument for inoculation with irido-platinum point flattened out; (*c*) alcohol lamp for sterilizing the instrument.

One hour later all the three lesions of the epidermis will show uniform slight hyperæmia, but while this will disappear after a few hours at the control scratch, there will appear a round hyperæmic elevation and infiltration around the two inoculated scratches, if the individual is tuberculous. The diameter of these specific infiltrates varies between 3 and 50 mm. and may occasionally lead to a somewhat more extended hyperæmia in the vicinity of the actual inoculated area. In the majority

of cases the reaction will be distinctly visible in twenty-four hours, when in some cases it has already its climax. The best opinion can be formed of the reaction after forty-eight hours, and for this reason I always have the inoculated children brought to me after the lapse of that time. I should not omit to mention, however, that there are cases in which a decision as to the positive nature of the reaction cannot be arrived at until three, four or more days have elapsed.

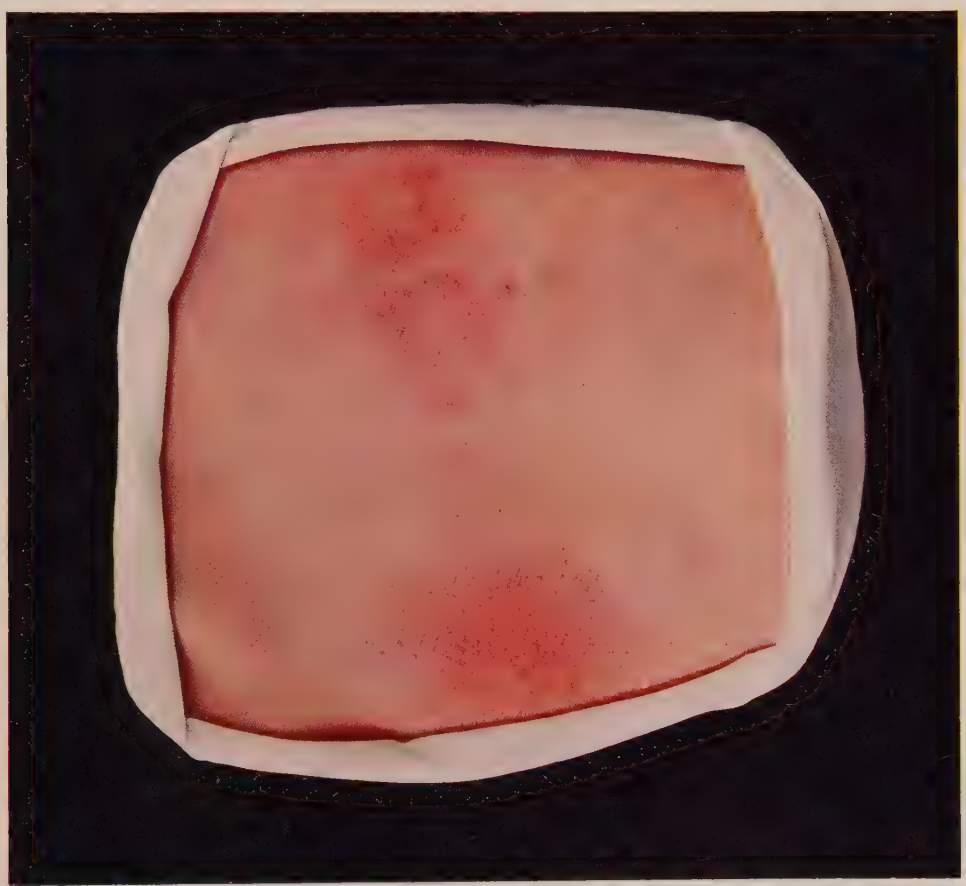
The appearance of the reaction varies with the length of time that was required for its occurrence. In some cases it may be bright red, very prominent and considerably raised above the level of the skin, with a central indentation showing the actual spot of inoculation; in other cases it is almost bullous; in others again it is hardly raised at all, dull brown in color, and hardly showing any traces of a true inflammation, so that the reaction gives rise to the widest variations. It is the control incision that but rarely leaves a doubt as to whether the reaction is positive or negative.

The diagnostic value of von Pirquet's cutaneous reaction is enormous, most especially so in children. The positive reaction not only indicates the presence of a progressive tuberculous affection, but also that the positively reacting individuals are allergistic to tuberculosis, *i.e.*, that they must have been infected with tuberculosis at some time or other. In view of the frequency of small tuberculous foci in adults, the positive findings of cutaneous reaction, therefore, reveal in their case just as little, as say the febrile reaction of a subcutaneous injection. In children, however, matters are different, seeing that there are but rarely latent tuberculous foci. The younger a child is, the more important is the positive result of Pirquetisation.

The advantages of Pirquet's procedure over the subcutaneous method are the following: Simplicity and rapidity in both inoculation and results, there being no injections or taking temperatures; absolute harmlessness, there being neither fever nor subjective or objective manifestations; only one or at the most two inoculations as compared to the necessity of repeated subcutaneous injections with increasing doses; nor does the presence of fever interfere with Pirquetisation. The disadvantages are very slight, considering the value of the reaction: In miliary tuberculosis, cachexia and near the end of life Pirquet's method will fail, but in these cases the subcutaneous injection is but rarely instituted. Besides, if cachectic individuals should recover, an originally negative reaction may turn to positive, as I had myself occasion to observe in one case. In measles, shortly before the eruption of the exanthema and until about the ninth day after its disappearance, there is seemingly no more allergy, so that the reaction even in the tuberculous will be to all intents and purposes negative. This is probably also the case in croupous pneumonia.

PLATE 38.

Cutaneous tuberculin reaction (Pirquet). *a*. Strong positive reaction. The test is made on the chest and the plate shows the reaction after 48 hours. The control spot without tuberculin can no longer be seen. *b*. Slight positive reaction. The test is made on the arm and the plate made 48 hours later.



Percutaneous tuberculin reaction. Pure tuberculin is rubbed in the skin over the chest. The reaction after two days is seen over the left chest and after five days over the right chest.

Again, the reaction may under certain circumstances be negative at first and turn to positive on repeating the inoculation, because the first inoculation has sensitized the subject by the introduction of traces of tuberculin (Pirquet). For this reason I have made it a rule for some time past to repeat the cutaneous inoculation if the reaction should be negative after eight days, and ever since this rule has been followed, the reliability of the reaction leaves nothing to be desired. This, however, alters nothing in the fact that the subcutaneous injection is far superior to cutaneous inoculation.

It may, however, be admitted that a positive reaction may occasionally be simulated in nontuberculous children. With increasing experience these misinterpretations may be avoided; nevertheless, there are individuals so "reactable*" that the introduction of any heterogeneous substance, which includes tuberculin, causes a slight reaction. Here again repetition of the test is the best means to avoid a pitfall. If the individual is tuberculous, the second reaction will be the more pronounced; otherwise it will either not occur at all or only to a very slight extent.

A positive reaction will completely disappear in a few days, weeks or months. If, as is sometimes the case, there is much itching at the climax of manifestations or in the healing period, the application of an indifferent ointment may be necessary. It may also be possible, as was pointed out before, that in subcutaneous injection the places where previously cutaneous inoculation had been practiced, will again flare up.

Pirquet's cutaneous inoculation should be applied in every case where there is the least suspicion of tuberculosis; it is the method of choice for the general practitioner. It is also well adapted to the requirements of wholesale examinations in schools, orphanages, etc.

Soon after Pirquet's reaction became known, numerous modifications and other forms of the allergy test were proposed, but the one inaugurated by Moro-Doganoff in which tuberculin is percutaneously applied, is the only one of practical importance. Moro terms the same "*salve reaction*" and employs the following ointment:

R. Tuberculin. Kochi..... 5 c.c.
Lanolin. anhydric..... 5. 0
M. fiat unguent.

Seeing that 5 c.c. of tuberculin weigh 6 grams, this tuberculin ointment would contain about 60 per cent. of tuberculin in weight. A little of the salve, the size of a pea, is, according to Moro's instructions, rubbed with the finger into the skin (back, chest or abdomen) for about a minute; in my own opinion a glass rod, thickened to a knob at the end, would be preferable for this purpose. The diameter of the treated part

* By "reactability" I mean a condition of increased irritability in which patients show a certain hypersensitiveness to irritations, to which others, or the same individual at a different period, do not perceptibly react.

of the body should not exceed 5 cm. and the place be kept exposed for ten minutes. A protective bandage is not required. The typical reaction consists in the appearance of more or less numerous, red, nodulous efflorescences at the place of inunction, somewhat resembling tuberculids.

The French investigators Lignéres and Berger, also Lautier, have used diluted tuberculin (1:100 aqua) instead of the salve; personally I have used pure tuberculin for percutaneous reactions.

The advantage of these methods of application consists in avoiding inoculation of which some people stand in dread. In certain cases it may even be possible to obtain the reaction without the knowledge of the patient or his family and to save them all anxiety in spite of positive findings. In regard to reliability, the percutaneous reaction is but little inferior to the cutaneous method, although the reactions it produces, especially when pure tuberculin is used, are sometimes more violent than one would like to see.

Intracutaneous reactions, recommended by others (also the Auriculo reaction of Tedeschi, which has nothing to do with the present subject) have not met with much appreciation and hold the middle between the subcutaneous and cutaneous application of tuberculin.

A direct warning, however, should be sounded against the so-called ophthalmo-reaction or conjunctival reaction, introduced into the diagnosis of human beings by Calmetti and by Wolff-Eisner. The reaction is obtained by instilling a drop of diluted, glycerin-free tuberculin (1 : 100 or 1 : 200 water) into the conjunctival sac near the inner canthus. In the tuberculous it will cause a reactive conjunctivitis. The method has no advantages whatever over the cutaneous, and so many untoward manifestations have been observed in connection with it that it must be refused admittance into pediatric practice.

Other biological methods for the diagnosis of tuberculosis (agglutination, complement fixation, serum precipitation through bacterial lipoid substances (Stoerk), serum activation through hæmolysis of cobra poison and horse blood (Calmetti) need not be discussed as being outside the scope of this handbook. Interesting though their perspective may be, they have not yet passed beyond the stage of laboratory experiments.

Prophylaxis.—In considering measures of prophylaxis we shall first speak of the general precautions which should be taken to protect all children, and then of the special precautions which those should take who are predisposed to tuberculosis either by heredity or by their surroundings.

1. *General Precautions:* (*a*) increasing the powers of resistance of the body, (*b*) care that the child be subjected to the contagion of the tubercle bacillus as rarely and as late in life as possible.

(*a*) As regards increasing the powers of resistance, it would carry us too far afield to repeat what has already been said in the general part of this work. Of prime importance in this connection is breast-feeding. *A child nourished at the breast has greater resistance against all infections, including infection by the tubercle bacillus.* If artificial feeding be unavoidable, by all means, let it be carried out rationally, as regards quantity. Overfeeding as well as underfeeding during infancy weakens the protective agencies of the body. A mixed diet in which green vegetables have their proper share, must be begun at the proper time.

Alcohol paves the way for tuberculosis in childhood as at other periods of life. It should be absolutely excluded, forbidding even a glass of beer or medicinal wine. In order to protect the child against tuberculosis, its body should be hardened, its muscles made firm by exercise, and its lungs developed.

Anæmia, which is found more often among the pampered children who idle indoors, must be treated by dietetic measures. Furthermore, great attention must be paid from early infancy to disorders of the upper respiratory organs. Any catarrh of the nose or throat should receive prompt treatment; enlarged tonsils and adenoids should be removed early.

(*b*) In the prevention of infection a good general rule is that "a priori every person is suspected of having tuberculosis." Strangers should not be allowed to fondle children, especially during infancy, and above all, kissing should be prohibited. Tuberculosis should be borne in mind when selecting a nurse. Her family history should be considered as well as her own physical condition, and if there is any doubt, resort should be made to the tuberculin test. The choice of the other servants is of equal importance. *Any one suffering from an active tuberculosis should not be tolerated in the vicinity of children.* Cases where a phthisical nurse has infected a child of healthy parents are by no means unheard of. Midwives ought also to be examined for tuberculosis. Later in life, children may be exposed to this infection by their teachers or fellow pupils. Institutions that farm children to private individuals should see to it that there is no danger from this source.

When people change their residence, they should always consider the possibility that the previous tenant may have had tuberculosis, and clean or disinfect accordingly. These precautions are recommended for summer resorts and watering places. Such objects as retain the dust, *e.g.*, carpets, upholstered furniture, should be exposed to the sun before they are used, or better still, they should be entirely dis-

pensed with in children's rooms. Frequent sunning and ventilation will help to exterminate any tubercle bacilli that may be present. Creeping children should not be permitted to wander about, but should be confined to a small enclosed part of the room which has been covered with a clean sheet.

From earliest infancy we ought to combat the mischievous habit children have of putting everything into their mouths and of sucking their fingers. Nipples or "pacifiers" are a cause of many diseases, including tuberculosis, as we can readily understand when we see them taken from the dirty floor and put into the child's mouth. Another habit that should not be tolerated is the tasting of the milk by the mother or by the nurse, either by putting the nipple or the spoon into her mouth before giving it to the child.

Children should be kept away from people who cough. They should be taught cleanly habits, such as washing their hands before eating, for the nails are a favorite site for the deposit of dirt and bacteria.

Although human beings are by far the most frequent source of contagion, tuberculosis of cattle must be taken into consideration.

It is a disgrace to be compelled to admit that a large proportion of our milch cows have tuberculosis, and that their products, milk, cream, butter, meat, etc., are not without danger. We should therefore give infants only such milk in the raw state as comes from carefully inspected cows (frequently repeated tuberculin tests). Prophylaxis against tuberculosis without guarding against the evils of tuberculous cattle is a vain endeavor.

We should also take care that the milk of healthy cattle is not contaminated, an occurrence which is by no means rare. Therefore no one suffering from tuberculosis should be allowed to handle the milk at any stage.

Recently Behring has introduced a vaccine which promises to accomplish the immunization of cattle against tuberculosis. For man, however, no such means has been discovered.

2. *Special Prophylaxis for Children Predisposed to Tuberculosis.*— Every tuberculous individual who marries and has a family assumes a great responsibility. No person whose tuberculosis is not positively healed should be encouraged to marry. A child born of tuberculous parents, especially if the mother is affected, should be taken away from its parents immediately if we wish to provide for its future welfare. However, this radical measure will never be complied with unless the mother is in an advanced stage of tuberculosis. The most we can accomplish is to give the mother warning and advice.

How shall we nourish the child? Where the social conditions are good in every particular, I recommend the employment of a good wet-nurse. However, such instances are the exception and generally

the child must be fed with cow's milk. Only when the mother's tuberculosis is incipient can we risk an attempt at maternal nursing.

From the standpoint of the tuberculous mother, it is far more injurious for her to become pregnant again after a short interval than it is for her to nurse.

It is very true that occasionally tubercle bacilli have been found in the milk of tuberculous women. However they are few in number and play an unimportant part when compared to the many cases of infection of the child by the tuberculous mother in the crowded quarters of the poor. This is especially true where the mother prepares the infant's milk.

If the tuberculous parent be the father, then the child should surely be nursed by the mother. Theoretically the father should be separated from the child but in practice this is rarely feasible. It is principally among the poor that our good advice is difficult to follow. When the father is in the advanced stages of the disease and thus unable to support the family, the mother is compelled to become the bread-winner. The father in his turn attends to the household and to the children, and becomes a dangerous source of infection.

Children who have been subjected to tuberculosis must be reared with especial care. Every catarrh of the upper respiratory passages must be given particular attention, and infectious diseases such as measles and whooping-cough must be carefully guarded against. Mental and physical strain should be avoided. Nourishment and physical development are very important. Under some conditions, climatic measures exert a good prophylactic influence. In the summer such children should be sent to the sea-shore for a period of at least six or eight weeks. Such outing should be repeated and in some cases prolonged for months or even years. Mountain air is likewise beneficial. Tonics are also of value, especially arsenic when prescribed in the form of some natural mineral water. Iron may be used, preference being given to non-alcoholic preparations. At times a "Mastkur" or forced feeding, may be of benefit.

Finally we must repeat that a successful campaign against tuberculosis can be waged only if we prevent infection during childhood. For it is during this period of life in the great majority of cases that the infection takes place, although the disease may not become manifest until later in life.

Treatment.—As yet we know of no specific treatment. We hope for the best from Behring's latest investigations, especially his "tulase." Koch's tuberculin has a curative effect in some cases, but it is not widely applicable, and is valueless in generalized tuberculosis. In spite of these therapeutic deficiencies we must not be pessimistic, for tuberculosis is in certain stages a curable disease.

II. SPECIAL PART

We now consider the different clinical manifestations of tuberculosis in childhood. These are general or local.

A. GENERALIZED TUBERCULOSIS

This includes the tuberculosis of infants and the miliary and submiliary forms of the disease.

1. INFANTILE TUBERCULOSIS

The tuberculosis of infants deserves especial consideration, as it generally differs in its pathology, clinical course, and prognosis from other forms of the disease. For this reason we consider it separately.

Occurrence.—Tuberculosis is very frequent in infancy. The difficulties of diagnosis and the lack of autopsies render statistics of doubtful value as to its frequency. Among 532 autopsies of infants, I have met with tuberculosis 36 times as follows:

Age.	Number of Autopsies.	Tuberculous.	Non-Tuberculous.	Percentage of Tuberculous.
0–3 months	277	6	271	2.2
4–6 months	154	13	141	8.4
7–12 months	101	17	84	16.8
Total	532	36	496	6.8

From the above table we see that tuberculosis is uncommon during the first few months of life. Generally more time is required to cause death. The second quarter of the first year contains a greater number, and the second half year shows nearly 17 per cent. of tuberculous cases. My figures are rather below the average, *e.g.*, 10 per cent. the percentage of tuberculosis given by Finkelstein for the first year. This is due to the peculiar nature of my material, which includes many premature babies, cases of sepsis, etc. [These figures cannot be regarded as showing the frequency of tuberculosis in infancy, as it is now known that tuberculosis may be present, especially in the cervical, bronchial, or mesenteric lymph-nodes and not manifest itself macroscopically or even microscopically. The only exact test is the biological one, namely, injecting the suspected material into guinea-pigs. It is certain that the above figures would be still larger if such latent cases were included.—H.]

Etiology.—In this connection we must refer to what has been written above. However we must emphasize the fact that the infant is very susceptible to infection immediately after birth. Frequently we can trace the source of the infection to a parent or to the nurse. Milk does not play an important rôle in the genesis of the disease as it is generally cooked previous to being used.

Pathological Anatomy.—The characteristic of tuberculosis of infancy is the rapid generalization of the disease. I have never seen

a case come to autopsy where the tuberculosis was localized in one organ. In the early stages there occurs a dissemination by means of the blood, due to the breaking down of a primary lesion which involves the intima of a vessel, or to a focus rupturing into a neighboring blood vessel.

The type of tuberculosis is miliary, submiliary, or nodular, such as we find in the monkey. The latter is due to the rapid growth and early confluence of the miliary tubercles. The tissue of the infant is evidently an excellent culture medium for the bacilli. There is also a striking lack of reactive changes surrounding the lesions. The lungs and the bronchial lymph-nodes are regularly the most involved. The former besides showing miliary and nodular tuberculosis are often the seat of an acute tuberculous pneumonia. The conglomerate tubercles often break down and form cavities, which are by no means exceptional (7 in 20 cases, Geipel). In fact we may find true sequestræ lying within the cavities.

The bronchial lymph-nodes and spleen are also regularly involved. The liver, mesenteric lymph-nodes, and intestines are very frequently affected. The tonsils (7 in 17 cases), stomach, meninges, bones, etc., are not rarely the seat of tuberculosis.

Symptoms.—The symptoms of the tuberculosis of infants are manifold and variable. They present nothing characteristic of the disease. The general appearance of an infant suffering from tuberculosis is that of a mild marasmus. One of the first symptoms is that the child ceases to gain in weight. On the other hand, we do not always find a marked emaciation; on the contrary, some children, especially those in the first months of life, remain fairly well nourished. Indeed we must remember that, under appropriate diet, the infant afflicted with tuberculosis may even gain. This I have repeatedly seen demonstrated in nursing infants. When they begin to have persistent fever and cavities develop in the lung we find a sudden loss of weight. Not rarely, however, the disease takes a rapid course and the children die before they have lost materially in weight.

The appetite is generally lessened in the early stages. The accustomed food is refused and in spite of all efforts the infant will not take its nourishment regularly. In some cases, enlargement of the cervical lymph-nodes or of those situated about the œsophagus may cause pain in swallowing (see Plate 34 c).

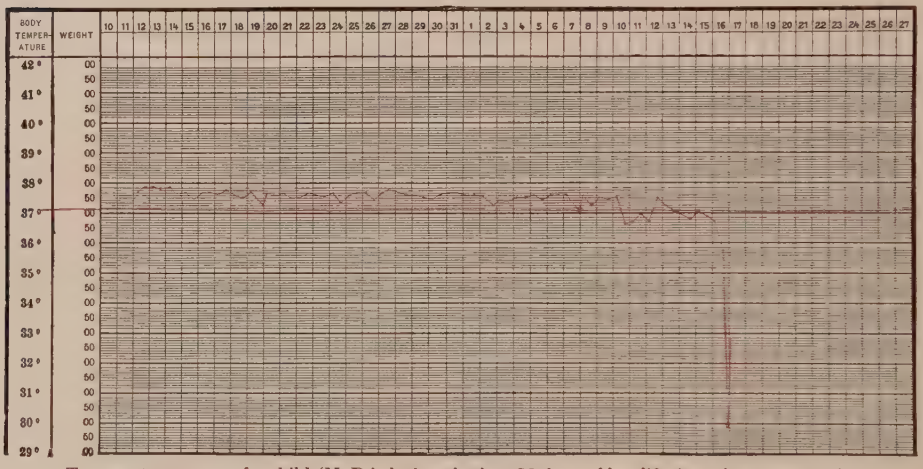
The fever is not of a regular type, and may throughout the disease be absent or at least remain very slight. The following illustrates this point:

M. B., born July 7th, admitted on August 10th, 1901, for ocular blennorrhœa and perforation of the left cornea. Died on September 17th, 1901. Mother had tuberculosis. During the infant's 39 days stay in the hospital its temperature remained almost normal (see Fig. 148). Weight on admission 2330 Gm., falling to 2000 Gm., on artificial feeding, and, as the result of changing to human milk, gradually

reaching 2310 Gm. on the day of her death. No pulmonary symptoms, no cough. Sudden death with symptoms of collapse. Autopsy showed: submiliary, miliary, and larger tubercles in the lungs, beginning tubercular pneumonia, cheesy bronchial lymph-nodes, miliary tuberculosis of the spleen, liver and kidneys, tuberculosis of the retroperitoneal lymph-nodes.

Nevertheless, continued taking of the temperature, especially when it is done every two hours, is of value in making the diagnosis. We find that the variations day by day are greater than we are accustomed to note in children. At one time the rectal temperature will be subfebrile, at another it will be 97° F. In other cases the temperature may suddenly shoot up to 102° F. or even higher, and may thus give the alarm. In the last stages of the disease we generally find an irreg-

Fig. 149.



Temperature curve of a child (M. B.) during the last 38 days of her life (rectal temperature).

ular remittent fever corresponding to the involvement of new areas. We frequently meet with a continuous fever in tubercular pneumonia.

The skin of tuberculous infants often presents a striking appearance. It is frequently of exceptional dryness, so much so that this may be the first sign to awaken suspicion as to the nature of the illness. Again we may find tuberculids, lichen scrofulosorum, scrofuloderma, and especially a tuberculous folliculitis, which even in infants may present the appearance of a sluggish furunculosis.

Of diagnostic importance are the small nodules, not as large as the head of a pin, situated beneath the cutis, most often in the umbilical region. These may also be present in an atrophic condition not dependent on tuberculosis. I have seen tuberculous ulcers about the rectum mistaken for syphilis. Careful examination of the skin cannot be too strongly urged, as it very frequently offers important diagnostic aid.

Examination of the lungs reveals varying conditions. We may find

nothing but a slight tympany over both lungs, accompanied by some intensification of the respiratory murmur. This may be expected in miliary tuberculosis where there is a diffuse dissemination of tubercles. If the tubercles conglomerate, and there is a definite invasion of the pulmonary tissue, we find slight dulness and especially a sense of resistance on percussion. Ausculation reveals diminished or slightly bronchial breathing.

Where a pneumonia, tuberculous or otherwise, is superadded to the miliary tuberculosis, we hear fine crepitant or subcrepitant râles, which may be more or less coarse according to the extent of involvement of the bronchial tubes. Not rarely, especially at the onset of a miliary tuberculosis we may hear diffuse coarse rhonchi.

Cavities may be formed without evincing symptoms. However, at times I have been able to diagnose even small cavities. I have often heard loud bronchial breathing and the so-called "cracked-pot" sound, which changes in pitch when the mouth is opened. At times the excellent conductivity of the infant's chest wall leads us astray in interpreting the localization of the lesions.

Pleurisy is frequently found, as we should expect considering that it is almost always involved in miliary tuberculosis; it is frequently of the fibrinous variety, leading to early adhesions. This accounts for the fact that we rarely meet with true empyemata. Such areas as break into the pleural space become at once encapsulated, so that pleuritic friction sounds are of short duration.

Respiration is always accelerated in extensive tuberculosis; we may, however, not infrequently find a moderate degree of cyanosis. Cough may be practically absent. At the onset there is frequently a dry hacking cough; where there are greatly enlarged bronchial lymph-nodes we may have attacks of coughing resembling whooping-cough.

Infants do not expectorate. By tickling the epiglotis with the fingers we can excite a fit of coughing, so that by swabbing out the entrance of the larynx we may obtain some sputum for examination. We do not see the greenish yellow expectoration which we are accustomed to find in adults. Even where cavities exist we cannot expect to find characteristic sputum.

The digestive tract in many cases offers no symptoms. Digestion progresses normally, although where there is marked intestinal involvement we may have diarrhœa which persists in spite of breast-feeding. Palpation of enlarged and cheesy mesenteric lymph-nodes is possible only in case of greatly emaciated children. Tabes mesenterica is rare in infancy. When we do find enlarged mesenteric lymph-nodes these are frequently not tuberculous but due to other causes.

The spleen is generally enlarged and extends below the free border of the ribs for two fingers or more. The diagnostic importance of this

phenomenon is lessened both on account of the frequency of enlargement of the spleen in infancy and its frequent lack of enlargement in tuberculous individuals. The liver is likewise not infrequently enlarged, either on account of simple stasis, or through tuberculous involvement; in the latter case we may expect icterus.

The ears are often involved in the tuberculosis of infants. We meet with peristent and intractable otitis, multiple perforation of the drum, loosening of the ossicles and marked destruction of the bony structures of the inner ear.

The urine may be normal; but generally towards the end of the disease the kidneys become involved. We may then find tubercle bacilli in the urine, and almost always albumin and casts. However, tubercle bacilli may be present without involvement of the kidneys.

In spite of the rather frequent involvement of the meninges and even of the brain, cerebral symptoms are not prominent. True meningitic phenomena are rare in infants. Tubercles of the chorioid are occasionally seen. [Chorioidal tubercles do not generally appear until the miliary tuberculosis is well advanced. In some cases they alone may enable the clinician to make the diagnosis as to the nature of the meningitis.—H.]

Diagnosis.—The diagnosis may be established from the symptoms described above. Tuberculosis occurs at every age and must always be borne in mind.

The history should be given sufficient weight. A consideration of the general condition of the child combined with that of the physical examination does not frequently permit of a rapid and certain diagnosis. As regards the physical signs, I consider only one pathognomonic, namely, the finding of a pulmonary cavity. It is frequently difficult and sometimes impossible to demonstrate the presence of tubercle bacilli.

The bacilli should be sought for patiently and repeatedly. If there is a lack of expectoration, the method mentioned above may be resorted to.

The urine and stools should be examined in this regard. Sometimes we may find tubercle bacilli in the cerebrospinal fluid, in the absence of all signs of meningitis.

Where there is no fever, tuberculin should be used to determine the diagnosis. Especially in infancy may this test be resorted to, for the prognosis is so poor that we do not need to fear doing any harm, and, in the second place, young children bear large doses of tuberculin well. The temperature generally falls quickly to the normal, as we usually are dealing with uncomplicated cases. Where fever is present tuberculin cannot of course be used.

In the *differential diagnosis*, typhoid fever must be considered, as where this disease is prevalent it is very commonly met with among infants, and pursues an atypical course. The Widal reaction must be resorted to in order to establish a diagnosis. Chronic bronchitis and

chronic pneumonia may simulate tuberculosis; besides, I have frequently seen empyema mistaken for tuberculosis. However, in tuberculosis we do not find dulness of such marked intensity; in case of doubt the needle will decide. On the other hand, the other chronic pulmonary diseases can be differentiated only if the patient improves markedly or if, on the contrary, we find tubercle bacilli in the excreta. Finally, there are certain forms of sepsis that resemble tuberculosis. Furthermore, a toxic intestinal catarrh, if seen only for a short period and without the aid of a reliable history, may be mistaken for tuberculosis.

Sometimes the tuberculosis of infants proceeds without symptoms, and sudden death occurs, the cause of which is unsuspected before autopsy.

Prognosis.—The prognosis of tuberculosis in infancy is bad.

We do not know of a single case which resulted in cure. Indeed there is not a positive instance where a tendency toward the limitation of the disease was observed. The tissues of the infant do not seem to be able to respond by protective inflammatory reaction. The result is that the lesions do not become circumscribed nor calcified. The youngest child whose organs showed processes which may be characterized as defensive in nature was one 15 months old. In this case a zone of inflammation with the formation of new vessels surrounded the tuberculous area (Plate 35).

The duration of the disease is very variable. It may progress rapidly and towards the end assume a foudroyant form as we see in the acute miliary type of adults. It may progress slowly, lasting months. Therefore it is best not to venture to make a statement as to the possible duration of the disease even when the diagnosis is certain.

Treatment.—We can use only prophylactic measures, as there is no treatment for the disease. The two main prophylactics are breast-feeding and improvement of the congested dwellings of the poor.

We can hardly combat the individual symptoms successfully. If the fever is high, and the infant restless, we should resort to hydrotherapy, in the form of packs or lukewarm baths. The best antipyretic, should we wish to give one to an infant, is pyramidon given as follows:

Pyramidon, 1.0–2.0 Gm. (15–30 gr.), syrup, 30 c.c. (1 oz.), aquæ ad 100 c.c. (3 oz.) one half to one teaspoonful every hour until the temperature falls. Convulsions may make one wish to prescribe narcotics; in such an event, chloral hydrate 0.5 Gm. to 100 c.c. (7½ gr. to 3 oz.) may be given by rectum.

2. ACUTE MILIARY TUBERCULOSIS

Miliary tuberculosis resembles an acute infectious disease, and occurs at every stage of childhood. We meet with it in infants presenting the same picture as in adult life.

Etiology and Pathogenesis.—Miliary tuberculosis is almost never primary in origin. It follows some tuberculous focus in the body,—most commonly cheesy bronchial lymph-nodes. The primary focus may be recent or of long standing. Every person who harbors tubercle bacilli runs the danger of developing a fatal miliary tuberculosis. This development generally is spontaneous but may follow some operative procedure. All that is necessary is that the bacilli obtain entrance to the blood stream in large numbers, as readily happens when a cheesy lymph-node ruptures into a vessel.

The tubercle which causes the general infection may lie in the vessel (see Fig. 136) or as just mentioned may rupture from without into the blood or lymph stream. Naturally the blood vessels of a diseased lymph-node are most endangered.

About 8 or 10 days following the dissemination of bacilli, characteristic tubercles appear throughout the body. The sites of predilection are the serous surfaces, as well as the spleen, the lungs, the bone marrow, the liver, the kidneys, etc. *No organ and no part of an organ is immune from infection.* The number of tubercles varies, but is generally large. Following the primary dissemination, there may be a second or a third, and even more if the patient lives sufficiently long. This may be deduced from the various sizes and stages of development of the tubercles which we find at autopsy.

Symptoms.—The disease may set in acutely without any prodromal stage, and attack an apparently healthy child. At other times the child complains of indefinite symptoms for a week or more, is apathetic, lacks appetite, and may have an occasional rise of temperature, until suddenly the seriousness of the ailment begins to impress itself upon us. The fever quickly becomes marked but presents no characteristic curve.

In some cases the fever rises gradually, and remains high with remission of 1 or 2 degrees until death. However it may begin with a rise to 104° F. or over, and be characterized by marked and repeated remissions. The pulse is rapid in comparison with the temperature. If the meninges are involved early in the disease, we may find a slow or irregular pulse at the onset.

Percussion and auscultation of the lungs afford little aid in the diagnosis. At times there is a slight tympanitic note. Bronchitic râles point to involvement of the lungs. The breathing is rapid and a considerable degree of cyanosis may be present.

The cough may be very distressing and dry; in small children, however, it is frequently absent or of no moment. Expectoration when present is scanty. The spleen is almost always enlarged and is hard and firm in consistency. The urine at times contains tubercle bacilli and frequently gives the diazo reaction. Involvement of the meninges may

a *b*

a. Miliary tubercles and large caseous degeneration of bronchial glands.
b. Miliary tuberculosis in a 4-year-old child without apparent involvement of bronchial glands.
(Photographed from nature.)

lead to early cerebral symptoms. Indeed these may dominate the clinical picture to such a degree that one considers the case one of tuberculous meningitis.

The difference between tuberculous meningitis and miliary tuberculosis with meningeal involvement is generally not clearly defined. We should speak of tuberculous meningitis when the miliary tubercles are confined to the meninges with but one or at most a few tuberculous foci in the entire body. In true miliary tuberculosis there is to a certain extent a general dissemination of tubercles. In tuberculous meningitis the picture is distinctly cerebral in type; in the miliary form, death frequently intervenes before the cerebral symptoms are very marked. Miliary tuberculosis is equally prevalent throughout all stages of childhood, tuberculous meningitis is most common between the ages of two and six.

Diagnosis.—The diagnosis of miliary tuberculosis is certain only when we find tubercule bacilli. This however is not possible in most of the cases, for the sputum does not contain bacilli, as the foci do not generally communicate with the bronchi. Sometimes we may find tubercle bacilli in the urine, but failure to find them does not affect the diagnosis.

The demonstration of bacilli by inoculation of the blood into animals requires too long a period to render it of practical importance. Rarely there may be a sufficient number of bacilli in the blood to permit us to find them in blood spreads. We may, however, find the bacilli in the cerebrospinal fluid, especially in the characteristic web, in the absence of all cerebral symptoms. Failure of the fluid to react to Fehling's test points to an inflammatory process, generally tuberculous in nature.

The tuberculin test is of value only early in the disease, on account of the temperature in the later stages. Examination of the fundus of the eye should never be omitted, as sometimes chorioid tubercles are found.

Of the diseases which may offer difficulty as regards differential diagnosis we must place typhoid fever in the first rank.

At times diagnosis is impossible, especially as *typhoid fever* so often runs an atypical course in childhood. For example it may show no continued fever, on the other hand this is also true of miliary tuberculosis. I would never rely on the temperature to differentiate between these diseases. The large spleen and the diazo reaction are common to both, although absence of the latter points rather against typhoid fever. Even the roseola may be present in miliary tuberculosis. The lungs do not serve to differentiate the diseases. Involvement of the pericardium and pleura early in the disease, or meningeal symptoms, points rather to tuberculosis. The Widal reaction if positive decides in favor of typhoid fever.

Next to typhoid fever, *cryptogenetic sepsis* offers most difficulty in the differential diagnosis. Here again the temperature, spleen, and general symptoms do not aid us. Chills and marked variation of the temperature point to sepsis, but are of rare occurrence. The diazo reaction points to tuberculosis; on the other hand, hæmorrhages of the skin or mucous membrane favor the diagnosis of sepsis.

I once saw a case of *sinus thrombosis* with such indefinite symptoms that it was regarded as miliary tuberculosis to the very end.

Lobular pneumonia and capillary bronchitis may be mistaken for miliary tuberculosis or vice versa. In this regard we should consider that in the latter disease the rapidity of respiration and dyspnœa are in marked contrast to the intensity of the pulmonary symptoms. The diazo reaction speaks in favor of tuberculosis.

I have also seen *severe influenza* with meningeal involvement resembling miliary tuberculosis.

Localized tuberculosis of the bronchial lymph-nodes with caseous formation may cause difficulty in diagnosis.

Prognosis.—The prognosis of miliary tuberculosis is bad. In pronouncing the diagnosis you doom the child to death. The disease lasts a varying period. Death may ensue after 8 to 10 days or it may be postponed for 4, 6, or even more weeks.

Treatment.—There is none. We may give symptomatic treatment; chloral hydrate as mentioned above, or cold compresses or ice bags to relieve headache. Hydrotherapy, prolonged baths at 30–32° C. (86–90° F.) often quiet the patient. Free access of fresh air should be allowed in order to relieve the dyspnœa. The use of oxygen inhalations may be indicated.

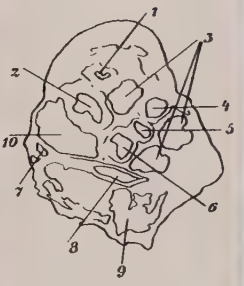
B. LOCALIZED TUBERCULOSIS

1. TUBERCULOSIS OF THE BRONCHIAL LYMPH-NODES

The bronchial glands in children are certainly a locus minoris resistentiæ. The bacilli must here gain an easy entrance and furthermore must flourish at this site. *We find the bronchial lymph-nodes almost without exception involved in every tuberculous child.* In very many cases we can easily demonstrate that these areas are the oldest in point of origin, and that the spread of the disease throughout the system or to the lungs or meninges originated from this focus.

It is questionable whether isolated bronchial lymph-node tuberculosis is as common as one would imagine from a superficial post-mortem examination. A more careful examination will often disclose small areas in the lungs which are easily overlooked. However, the main feature, from an anatomical as well as from a clinical point of view, is the tuberculosis of the bronchial lymph-nodes, as the small pulmonary foci, even if primary, are frequently completely healed.

a



b

c

a. Typical tuberculosis in infancy. Round caseous masses spreading from the bronchial glands and miliary tubercles.

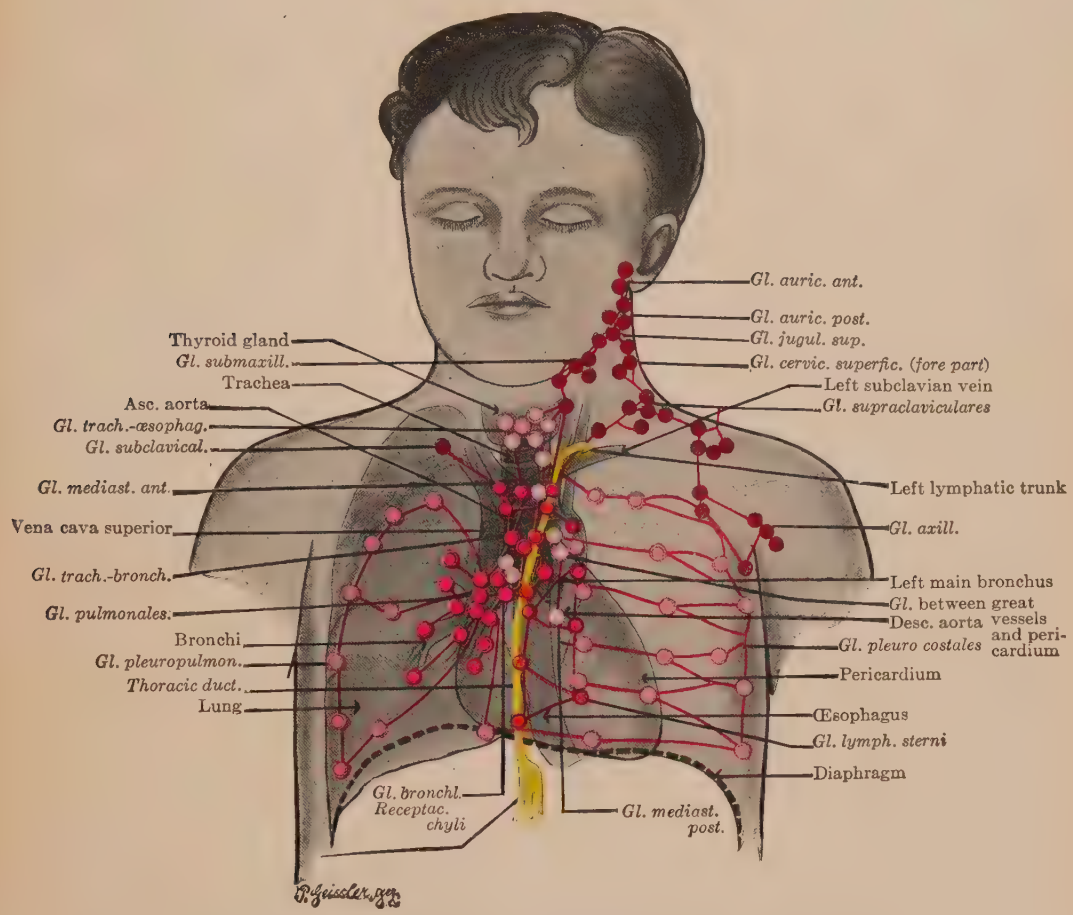
b. Bronchial glands and miliary tuberculosis in an infant. Attention is directed to the size of the tubercles.

c. Transverse section through the neck of a tubercular infant at the level of the sternal notch. 1, œsophagus; 2, trachea; 3, caseous glands; 4, left subclavian artery; 5, right subclavian artery; 6, innominate artery; 7, junction of right innominate vein with superior vena cava; 8, innominate vein; 9, thymus with caseous spot; 10, enlarged gland with a few caseous spots. (Photographed direct from nature.)

On the other hand we have *unquestionable cases of isolated tuberculosis of the bronchial lymph-nodes,* indeed Weléminsky has lately expressed the opinion that glandular involvement *always* precedes involvement of the organ itself, even in the case of the lung and its lymph-nodes.

A careful consideration of the anatomical relationship is necessary in order to understand this question. The bronchial lymph-nodes com-

FIG. 150.



Bronchial and other lymph-nodes mainly affected in tuberculosis. (The dark-colored markings represent the most superficial, the light-colored the most deeply situated nodes.)

prise those lymphatic glands in the thorax which receive the lymph stream from the lungs and the bronchial system. As these nodes, however, are closely connected with other lymphatic glands of the thorax and the neck, we must consider them as well. There are three sets of bronchial lymph-nodes:

(*a*) *The tracheobronchial lymph-nodes* situated at the bifurcation of the trachea, one of which is situated in the angle formed by the separation of the main bronchi.

(*b*) *The bronchial lymph-nodes* situated along the main bronchi.

(*c*) *The pulmonary lymph-nodes* situated at the hilus of the lungs, also peribronchial in their arrangement, and extending to or into the parenchyma.

All three groups receive their lymph from the lungs, the bronchi and, in part, from the posterior aspect of the heart. Their enlargement leads most especially to pressure upon the trachea, the larger and middle sized bronchi, as well as upon the recurrent laryngeal nerve.

Other lymph-nodes to be considered are:

(*d*) The anterior mediastinal, about 12 in number, situated posterior to the sternum and around the large vessels, *e.g.*, in the space between the right innominate artery, in the concavity below the right subclavian artery, and in the concavity formed by the arch of the aorta.

According to Friedleben, the nodes lying below the concavity of the right subclavian are very frequently affected. The lymph entering these nodes comes from the anterior portion of the diaphragm and from the upper surface of the liver, as well as from the pericardium, the heart and the thymus. Their enlargement leads to compression of the great vessels.

(*e*) The posterior mediastinal lymph-nodes situated along the aorta and œsophagus and receiving the lymph from the œsophagus, posterior part of the diaphragm, pericardium and the liver. Enlargement produces compression of the œsophagus, or even of the aorta. All these nodes (*a–e*) are connected by anastomosis, so that disease of one set may be transmitted to another. They also connect with nodes lying outside of the thoracic cavity, of which the most important groups are:

(*f*) The tracheal and œsophageal lymph-nodes. These are covered by the sternothyroid muscle, and extend from the isthmus of the thyroid gland, down along the anterior aspect of the trachea, two or three being situated somewhat to the left on the œsophagus.

(*g*) The jugular lymph-nodes lying beside the internal jugular veins.

(*h*) The supraclavicular lymph-nodes lying above the clavicle and between the borders of the trapezius and the sternomastoid muscles.

(*i*) The superficial cervical lymph-nodes lying on the upper half of the sternomastoid muscle and below and behind the external ear.

(*j*) The submaxillary glands situated behind the chin.

All these nodes (f–j) communicate directly or indirectly not only among each other but also with the true bronchial nodes.

[This important fact is not definitely established. Recent experimentors have been unable to demonstrate by means of the injection of colored fluid into the cervical lymph-channels any connection between the cervical and bronchial lymph-nodes. Again clinical experience shows that we may frequently meet with tuberculosis of the cervical lymph-nodes without a secondary involvement of the bronchial lymph-

nodes or lungs. It also shows that of the many cases of pulmonary tuberculosis in which the bronchial lymph-nodes are affected, few are complicated by a tuberculosis of the cervical lymph-nodes. These circumstances, experimental as well as clinical, must be weighed when we judge of the existence and importance of the anastomosis between the cervical and thoracic lymph systems.—A. F. H.]

The question as to how the tubercle bacilli gain admission to the bronchial lymph-nodes allows of two answers: either they gain entry to the lungs by means of the venous blood current or by the air and are carried thence to the lymph-nodes by the interlacing lymph capillaries, or they follow the direct path from lymph-nodes outside the thorax, more especially the cervical chain. We must also not overlook the fact that following a tuberculosis of the bronchial lymph-nodes a retrograde current may be set in motion which will bring about the involvement of nodes situated external to the thoracic cavity.

Symptoms.—The clinical picture of tuberculosis of the bronchial lymph-nodes is by no means clear if we except those rare cases where the entire symptom-complex points to the diagnosis.

The onset of the disease is generally insidious. The condition of the child passes almost imperceptibly from one of health to that of disease. The appetite becomes poor, the cheeks lose their color, the child soon grows thin although it continues to grow in length, which makes its loss of flesh appear more marked. Irregular pyrexia at this time points to some systemic affection, but examination generally discloses nothing. In fact *the lack of cause for the change in the general condition of the child is truly characteristic of tuberculosis of the bronchial lymph-nodes.*

In other cases the course may be a different one. After a short preliminary stage, high fever may set in, the temperature remaining at 40° C. (104° F.) for weeks and gradually falling by lysis.

The fever curve is atypical, it may be broken by marked remissions or it may be continuously high. We meet with all the manifestations which accompany prolonged fever in children: loss of weight and strength, lack of appetite, apathy, etc.

In those cases where the nodes are much enlarged and form a large cheesy mass, we may be able to diagnose the condition by the *physical signs*, however, in this regard I am somewhat sceptical, as are also Widerhofer and Henoch. Dulness can hardly ever be absolutely determined as due to enlargement of bronchial nodes. Even large tumors may not cause dulness, owing to the resonance of the pulmonary tissue.

Two areas are especially accessible for percussion, the interscapular space at the level of the 2nd and 3rd dorsal vertebræ, and anteriorly over the manubrium sterni. In these locations an increased sense of resistance may also aid us in the diagnosis.

Auscultation generally reveals nothing on account of the excellent conductivity of the neighboring pulmonary tissue. In the interscapular space according to Seitz, rough harsh respiration, especially in expiration may be heard; Widerhofer states that this is more marked on the left side.

We should always try to feel a resistance deep down in the suprasternal space. Sometimes a mass of nodes may be palpated. Palpation of the cervical and submaxillary nodes may also be of aid in the diagnosis. However these nodes may not be enlarged in spite of, or notwithstanding, tuberculosis of the bronchial nodes.

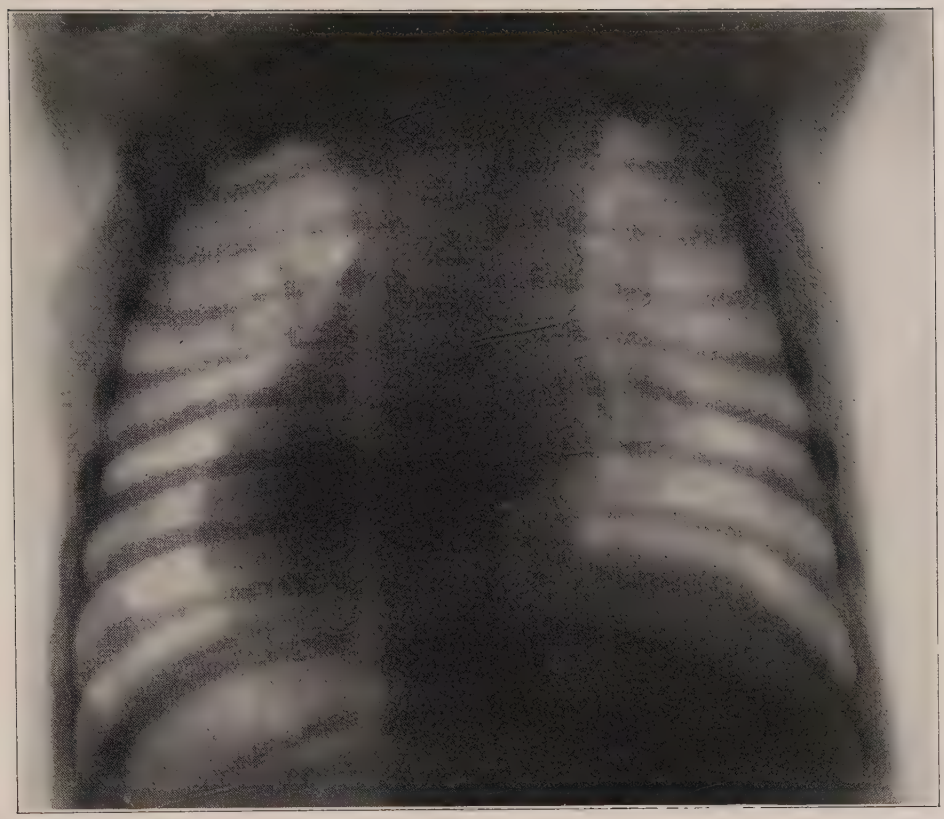
The cough is an important symptom and may be characteristic. It occurs in prolonged attacks, occurring perhaps at intervals of hours, and frequently resembles the paroxysms of pertussis. However there is no mucous, no vomiting, no regular nightly exacerbations. The attacks of coughing are probably caused by pressure of the enlarged nodes upon the vagi nerves.

We must now consider what may be designated as the indirect consequences of tuberculosis of the bronchial lymph-nodes caused by compression on the important organs in their immediate vicinity (see Plate 34, Fig. *c*). In the first place the trachea is exposed and may be almost flattened out by pressure. The result is a disturbance of respiration, dyspnœa, cyanosis and finally suffocation. If the nodes press upon only one bronchus, more or less of the lung may cease to functionate. Again, the œsophagus may be entirely occluded by pressure from without, resulting in pain, difficulty in deglutition, leading even to starvation. The blood vessels, more especially the large veins may be compressed, thus giving rise to all the symptoms of venous stasis (see Plate 34 *c*).

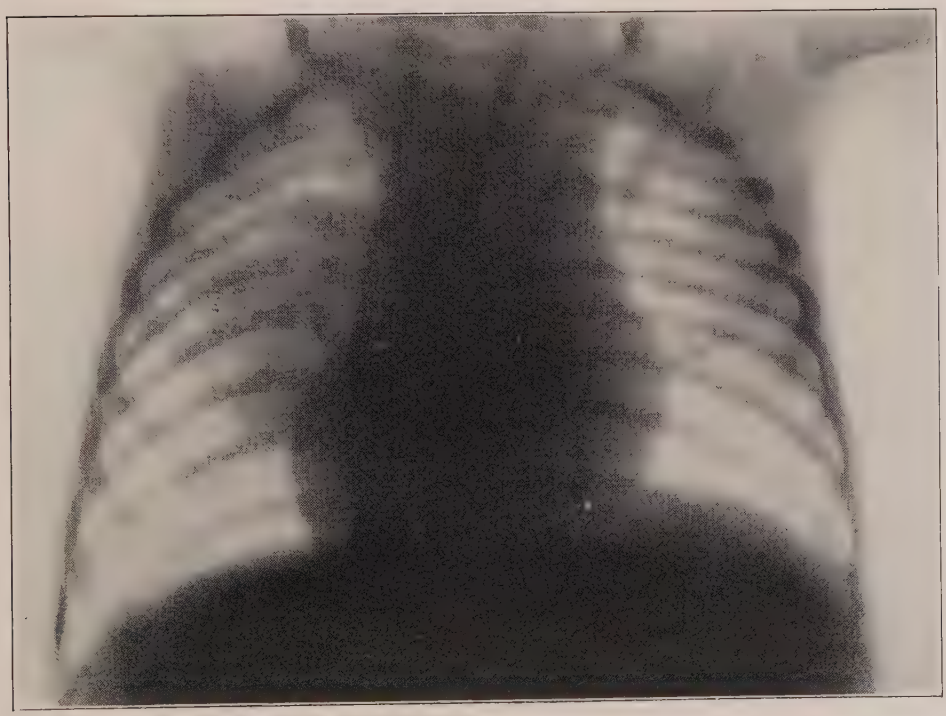
Course.—The course of tuberculosis of the bronchial lymph-nodes is variable. The disease may remain stationary; the cheesy nodes may become encapsulated or calcified. Nevertheless such a tuberculous node existing in the human body cannot be disregarded, especially if the affected individual be a child. For at any time an accident or an intercurrent disease, especially measles or whooping-cough, but also scarlet fever or diphtheria, may light up the latent focus and endanger the entire body. The bacilli may be transmitted to the lungs, to the meninges, or throughout the body.

In other cases, tuberculosis of the bronchial lymph-nodes may lead by continuity or by a retrograde current to pulmonary infection, resulting in a tuberculous peribronchitis, a diffuse tuberculous pneumonia, or in a local process in the neighborhood of the cheesy nodes, especially those at the hilus of the lungs (see Plate 34, Fig. *a*).

The nodes may break into the surrounding organs. I have seen a sudden rupture into the trachea lead to the expectoration of masses of cheesy material; a rupture into the bronchi cause an aspiration



Tuberculosis of the bronchial lymph glands in a four-months-old infant.



Tuberculosis of the right apex in an infant nine and a half months old.

pneumonia; a rupture into the vessels lead to a miliary tuberculosis of the lungs or entire body. The œsophagus, pericardium, or pleural cavity may likewise be penetrated. Sooner or later in almost all these cases death ensues.

Diagnosis.—The diagnosis in the early stages is difficult. If, after many thorough examinations of a child, we are unable to find the seat of the disease, we may suspect the bronchial lymph-nodes to be the source of the trouble. Radioscopy sometimes enables the diagnosis in advanced cases. Tuberculin may be tried in some cases when there is no fever.

The typical paroxysms of cough are of diagnostic value where pertussis can be excluded. In advanced cases with stenosis of the trachea, where no history of the slow onset is obtainable, it may be difficult to differentiate the disease from diphtheria or even from a foreign body in the bronchus. Sudden onset of the disease with high fever may cause it to be mistaken for miliary tuberculosis.

Prognosis.—The prognosis is not bad so long as the focus is not too large and there is no caseation. Where cheesy degeneration has taken place, we generally have an unfavorable outcome, due to involvement of other organs.

Treatment.—The prophylaxis of tuberculosis of the bronchial lymph-nodes is that of tuberculosis in general. The treatment consists in improving the general condition of the child, which at times accomplishes a great deal. A diet rich in fat, varied in nature, containing a large quantity of fruits and vegetables, is to be recommended, and its results tested by regular weighing of the patient. The appetite may be stimulated by giving spicy articles of diet, or by arsenic, especially in the form of the natural arsenical waters.

Mud baths are to be recommended. Some recommend giving potassium iodide or inunctions of iodine-vasogen. A careful tuberculin cure in the case of patients with normal temperature is by no means futile.

In addition, we should resort to symptomatic treatment. Continued fever may sometimes be held in check for a long while by means of hydrotherapy, lactophenin, pyramidon or aspirin. When the nodes compress the œsophagus we should be most careful in the use of the stomach tube. At times the symptoms improve following rupture of the glands. Where a marked dyspnœa results, resort to a low tracheotomy and to the removal of the glands from the trachea may be indicated.

A few words may be added in this connection concerning tuberculosis of the cervical lymph-nodes. This is of frequent occurrence, at times following involvement of the bronchial nodes, but far oftener through infection from the mouth, from carious teeth, from scrofulous eruptions about the mouth and nose, etc. Compared to the enlargement of these nodes through pyogenic processes, the tuberculous involvements progress slowly. They may be merely as large as a kernel of

rice or a cherry but may also reach the size of a plum or become even larger. If these nodes tend to infect those more centrally situated, early operative removal should be considered. As long as the affected nodes remain isolated, only dietetic measures should be resorted to. At times these nodes reach such a stage of caseation, that the neck becomes virtually imbedded in cheesy masses. The reproduction in Plate 34 conveys an idea of this condition.

2. TUBERCULOSIS OF THE LUNGS

(*a*) *Tuberculous Pneumonia*

Tuberculous pneumonia may follow immediately upon specific infection of the lungs, or, as is more commonly the case, result from the accidental lighting up of a subacute or chronic tuberculous process. This condition represents anatomically an exudation into the alveoli, caused by the vital processes of the tubercle bacilli and its toxines. The pneumonic area may be miliary, lobular, or lobar in extent. The peculiar glassy appearance of the cut section of this form of pneumonia leads to its appellation of gelatinous. The rapid caseation of these processes point to their specific nature.

The **clinical symptoms** resemble those of a simple pneumonia. If the areas are scattered, a lobular pneumonia may be simulated; on the other hand, the sudden onset, chill, high fever, and physical signs may suggest a lobar pneumonia.

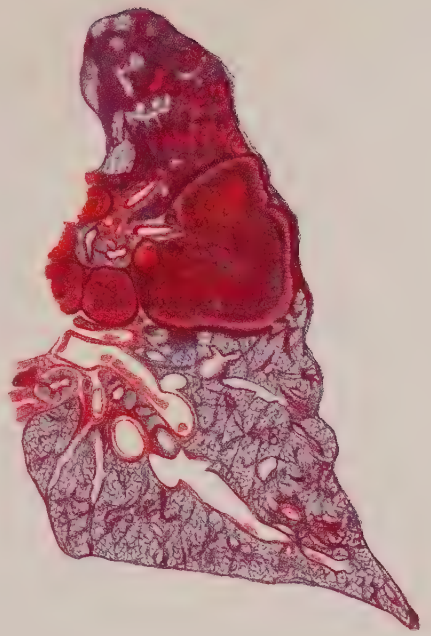
The **course** may be either a very rapid one, resulting in death after a few days, following continuous fever, marked dyspnœa, and terminal cardiac weakness, or, when caseation takes place, death after a few weeks, following high and irregular temperature and a great loss of flesh and strength. A complicating pleurisy is not uncommon.

A **differential diagnosis** from simple pneumonia is frequently very difficult. A history of previous tuberculous disease is very important. At times the absence of herpes and of râles redux and all signs pointing to resolution may allow us to exclude a simple pneumonia. In this form, as in the lobular variety, the demonstration of the tubercle bacillus clinches the diagnosis.

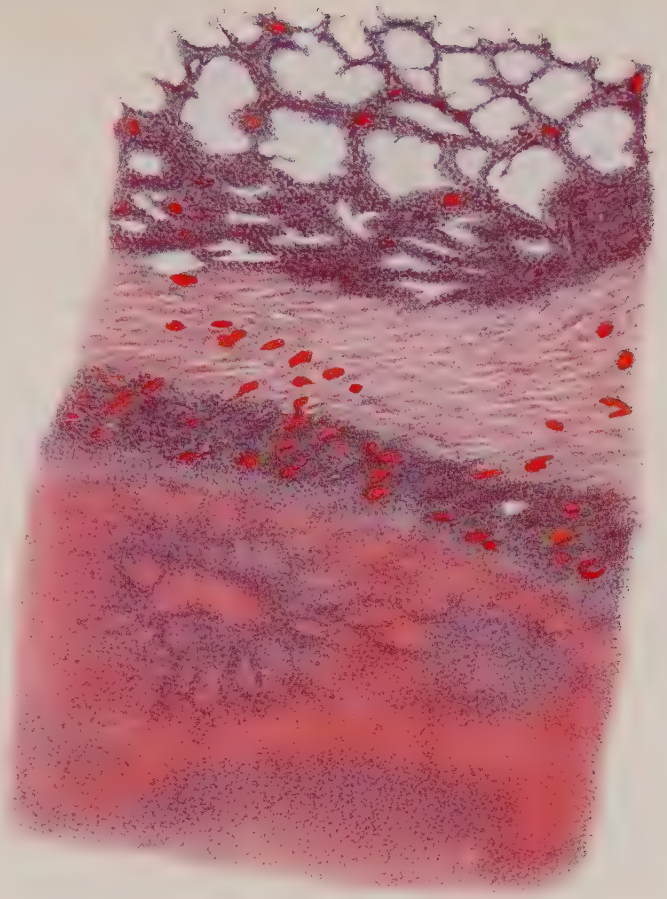
Treatment is powerless in this disease. Absolute rest in bed must be required and symptomatic treatment resorted to. The dyspnœa may be relieved for a time by oxygen inhalations. Morphine, codeine, etc., should be employed to allay the cough. Digitalis frequently relieves the subjective symptoms.

(*b*) *Miliary and Submiliary Tuberculosis of the Lungs*

This sometimes remains localized in the lungs. In such cases the symptoms are the same as we have described where the lungs are involved in a general miliary tuberculosis.



I. Section through left lung of baby Voigt (15 months old). Injected with formalin.



II. Section through one of the caseous masses in Section I.

(c) *Chronic Tuberculosis of the Lungs (Phthisis pulmonum)*

Whereas phthisis is very rare during the first years of life, and never occurs in infancy, we occasionally meet with it after the fourth or fifth year, and from then on it occurs with ever increasing frequency as we approach puberty. Its characteristics are a chronic course and the reactive indurative processes of the surrounding tissue.

Its **pathogenesis** is not certain. The majority of authors believe in an aërogenic infection, others however in a hæmatogenic origin. The former believe that the lungs are first invaded, the latter that the pulmonary infection is merely secondary to tuberculosis of the bronchial glands. On the other hand, Behring upholds an alimentary origin also for this form of tuberculosis, and, as I have said above, I favor this view.

There is no unanimity as to the meaning of the phthisical habitus (see Figs. 135–141) which we have described above. Some consider it merely a physical type predisposing to tuberculous infection, while others believe it to be an expression of an existing tuberculosis. The latter view is strengthened by the fact that we find tuberculosis, often latent, so frequently among children. According to this interpretation Freund's opinion that the lack of development of the first rib predisposes to pulmonary tuberculosis, would have no basis.

Symptoms and Course.—The onset is gradual, accompanied by a loss of flesh and strength, perhaps a cough, but an absence of all physical signs. In the early stage, the variations in the temperature, if this is taken at two hour intervals, may serve to indicate the nature of the trouble. It may be months before definite pulmonary symptoms are manifested. Meanwhile, the cough or expectoration, if the latter be present, is generally not characteristic.

At times an observant physician may be able to diagnose the condition before there are definite changes to be discovered in the lungs, by finding tubercle bacilli in the sputum. At times we may be able to hear dry or harsh râles in the morning, always in the same area, and percussion may reveal scattered tympanitic foci. However, the excellent conductivity of the thorax in children renders this difficult. We must remember that *in childhood the apices of the lungs are by no means so frequently the earliest parts to be involved by tuberculosis as is the case in adult life.* The first focus may quite as well be in some other area. But as we approach puberty we find that tuberculosis has a tendency to attack the apices first.

In spite of frequent and long remissions, the child gradually develops a phthisis which renders a diagnosis simple. We see the characteristic flattening of the chest, and the loss of weight, which however may not be marked if the fever is not high and a mixed infection has

taken place. The temperature shows irregular rises. The lungs give signs of scattered foci of tuberculosis, not necessarily involving the apices at first. Areas of dulness or of tympanitis are found and on auscultation *persistent catarrhal signs are heard, especially in the morning, the râles being sticky in character.*

Later cavities may develop, as the affected areas break down; this takes place readily and rapidly in childhood (see Plate 33). They manifest the same signs as in adults, namely, a tympanitic or "cracked-pot" note, rough bronchial breathing, and loud metallic râles. This is especially striking when, after a fit of coughing, accompanied by profuse greenish yellow expectoration, particularly in the morning, we find the above signs over an area where previously there existed dulness and absent respiratory sounds. Concomitant with the formation of cavities, we see marked failing in the general condition of the patient, and irregular fever, although in children apyrexia may exist almost until death. Numerous complications may now set in, and the patient generally dies of an acute tuberculous pneumonia or of gradual inanition.

Of the numerous complications just mentioned, hæmoptysis is relatively rare, whereas pleurisy is frequent. We often find a dry pleurisy at the onset, or even pleurisy with effusion, in fact the fluid in the early stages may be purulent or hæmorrhagic.

In older children the larynx is by no means rarely involved. The intestinal canal, subjected as it is to the swallowed sputa, frequently contains tuberculous ulcers, which cause a troublesome diarrhœa and sap the strength of the patient.

Diagnosis.—The diagnosis of early tuberculosis is very important, as upon this the question of therapeutic aid frequently rests. In this connection the family history is of importance and the possibility of exposure to infection. We must remember that this may have taken place years previous to the onset of the disease. An examination of the lungs should be repeatedly made, and we should note whether the catarrhal signs are always found in the same areas. *Well circumscribed pulmonary affections are always suspicious.* Repeated noting of the temperature will often give evidence of disease. The weight should be followed carefully. Sputum examination should be made repeatedly. We may even resort to attempts at causing the bacilli to multiply in the sputum or to injecting it into guinea-pigs. In the examination of the sputum especial attention should be paid to the presence of elastic fibres.

Tuberculin may be used if fever is absent. After its injection the râles often become more moist and bacilli may be found in the sputum.

Prognosis.—The prognosis is not bad if the disease is in an early stage. The fact that it has assumed a chronic form and has not developed into an acute miliary tuberculosis, points to a relative resistance of the child or to a lack of virulence of the bacilli. Indeed we fre-

PLATE 36.

FIG. 1.

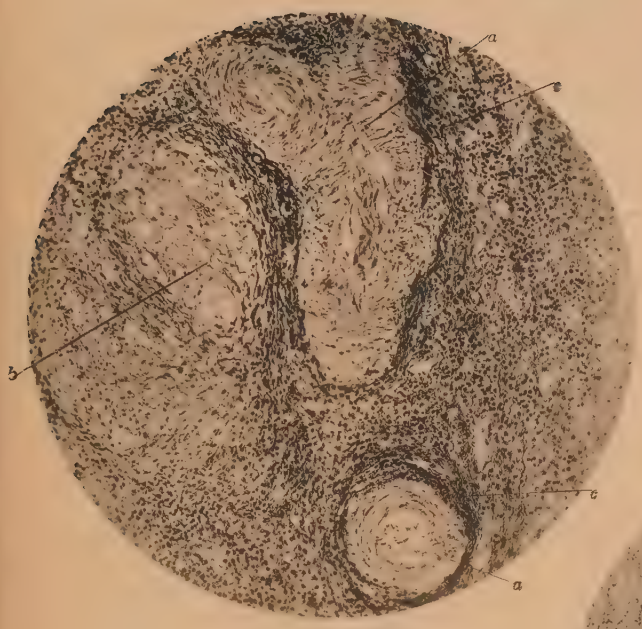


FIG. 2.

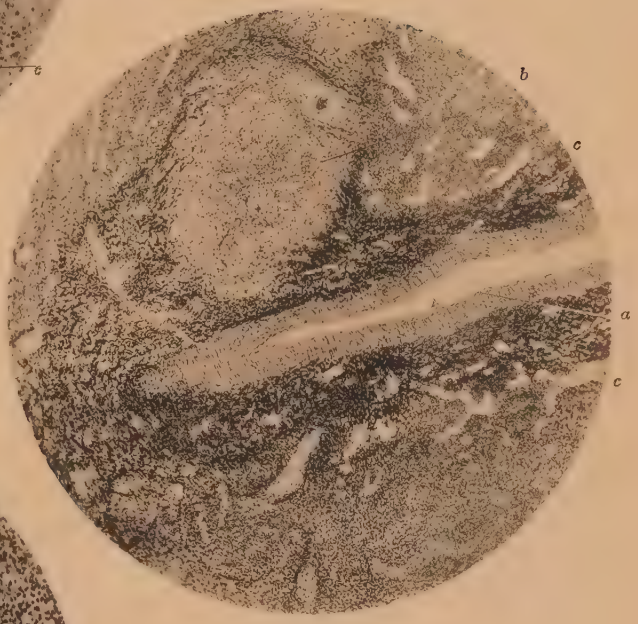


FIG. 3.

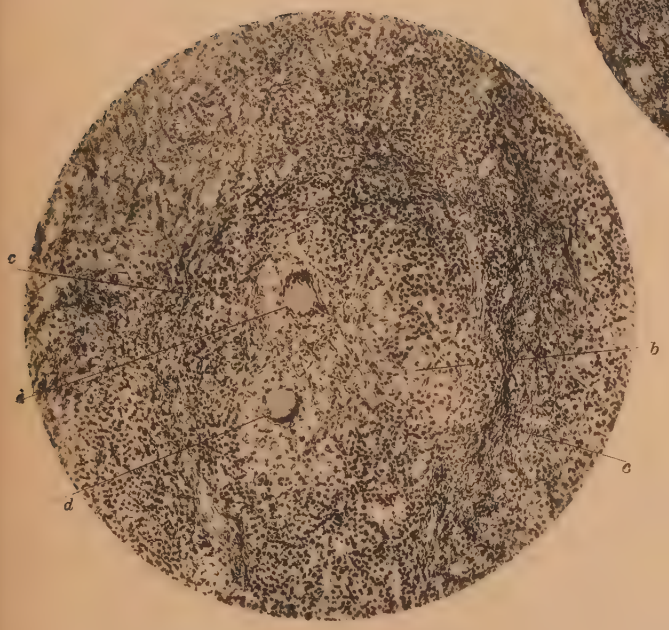


FIG. 1.—Cross and transverse sections of arteries in indurated tubercular granulation tissue. Thickening of the adventitia.

FIG. 2.—Fibrous tubercle whose capsule arises from the adventitia of a small artery.

FIG. 3.—Fibrous tubercle with two giant cells. Cellular connective tissue in the periphery.

a, artery. *b*, tubercle. *c*, connective tissue. *d*, giant cells.

1 and 3, Slight ocular magnification. 2, Strong magnification.

The preparations are from an indurated lung of a fourteen-months-old child who died from tubercular meningitis. *Van Giesen Stain.*

quently meet with a local cure, although permanent cures are seldom encountered. After some years, between the ages of 20 and 30, during the period of pregnancy, or as the result of some harmful employment, the spark is generally kindled anew and the supposedly healed focus gives rise to a fatal infection.

Treatment.—*Insipient tuberculosis is a curable disease.* We should treat suspected cases in the same way as those in which the diagnosis is definitely established. Phthisical children should not attend school, both for their own welfare and for the sake of the other pupils; with the exception of schools instituted especially for those afflicted with tuberculosis.

Hygienic and dietetic measures are of primary importance. The atmosphere should be free from dust; sea air is preferable in the early stages and high altitudes for all curable forms of the disease. We can expect little from a residence of a few weeks. If relapses are to be prevented, years must be spent in a favorable climate. Judicious hardening is a necessary part of the cure. As much time as possible should be spent out of doors. An especially valuable form of treatment consists in having the children lie in the open air, well covered and, if necessary, warmed by hot water bags. Sports, if not overdone, are also of benefit, even in the winter time. Respiratory exercises and gymnastics carried out under supervision should be a part of the daily routine. In prescribing the diet, increase of flesh is the most important consideration, and in this connection we should not pay so much attention to the quantity the patient consumes as to the quantity he utilizes.

I prefer a diet rich in fats, such as cream, butter, bacon, given with plenty of fresh vegetables, and raw fruit. Good raw milk is to be recommended, but all alcoholic beverages are to be avoided.

The following regime is an example of the kind to be recommended for cases of incipient tuberculosis: at 7 A. M. a cup of cocoa with cream, a roll with butter and some scraped ham should be given to the patient in bed. A half hour later the child should rise and take respiratory or gymnastic exercises. An hour previous to the next meal he should lie down, preferably in the open air. At 10 A. M. a second meal consisting of an egg and bacon, rye bread, a raw apple, pear or grapes should be given. Following this he should once more take exercise and rest in the open air. A half hour before lunch he should take about two ounces of beef juice or concentrated bouillon. The lunch may consist of rare meat, green vegetables. At 4 o'clock the patient is given tea or coffee with cream, and bread with butter, honey or marmalade. Finally at half past seven he has a light supper, a cereal, or omelet with preserves.

Exact regulations as regards sleep, rest, employment, recreation. diet and exercise have also their psychical value. Drugs may be given to increase the nutrition, such as arsenic or at times iron preparations. I do not use such as are supposed to affect the tuberculous process, as

for example creosote; however, this may be given with double the quantity of tincture of gentian. *It is a good rule to avoid unnecessary drugs so as not to disturb the appetite.*

Tuberculin is being used as a therapeutic measure, and has been especially recommended by Ganghofner.

We should begin with very small doses, 1/1000–1/100 of a mg. and increase only when we obtain no reaction. First we should preceed by doubling the dose, and later by increasing by 0.1–0.2 mg. until 0.01 Gm. is borne without reaction.

Symptomatic treatment is necessary in the incurable cases. Here too we should make use of the open air treatment, as it is very comforting to the patient. We know of very little to counteract the fever; at times lukewarm baths serve this purpose, or large doses of pyramidon, three grains hourly until the temperature falls. The disagreeable sweats are combated by sponging with dilute vinegar and then applying a simple powder, or one containing formalin. We do not need to resort to the use of atropine except in extreme instances, but we make use of the following prescription:

℞ Pyramidon camphorici ..... 5.0 ..... ℥iss
Syrupi ..... 35.0 ..... ℥i ℥i
Aquæ ad ..... 100.0 ..... ℥iii ℥ii
M.S.—2–3 teaspoonfuls at half hourly intervals before retiring.

The best treatment for hæmoptysis is rest, which is best obtained by means of morphine. In advanced cases narcotics (morphine, codeine) should not be spared, *e.g.*:

℞ Morphinæ hydrochlor. ..... 0.01–0.03 ..... gr. $\frac{1}{6}$–$\frac{1}{2}$
Syrup althææ ..... 35.0 ..... ℥i ℥i
Aquæ ad ..... 100.0 ..... ℥iii ℥ii
M.S.—Teaspoonful or half teaspoonful doses according to the age of the child.

To older children morphine is given in powdered form; the dose is $\frac{1}{2}$ mg. for each year of life:

℞ Morphinæ hydrochlor. ..... 0.015 ..... gr. $\frac{1}{4}$
Sacharri ..... 2.5 ..... gr. xl
M. Fiat pulvis. Divide in parts V.
S.—One powder at night.
The dose of codeine is three times that of morphine.
For diarrhœa, tannigen or tannalbin may be used.

3. TUBERCULOUS PLEURISY

Pleurisy may accompany any form of tuberculosis and should always be thought of in this connection. It may be of any variety, and is frequently the initial appearance of the disease in older children. The physical signs and temperature do not aid in the diagnosis. If the exudate shows no bacteria the process is probably tuberculous.

A careful examination of the sediment or coagulum of the fluid will reveal tubercle bacilli far oftener than is generally supposed. As a final resort we may inject the fluid into the peritoneal cavity or lactating breast of a guinea-pig.

A predominance of mononuclear leucocytes is said to favor the diagnosis of tuberculosis. It is certain that the presence of hæmorrhagic exudate points to this disease.

We may relieve the pain by warm applications, by painting the thorax with tincture of iodine, followed by applications of ointment, or by 10 per cent. iodvasogen. Serous exudate should be removed by aspiration, and purulent exudates by large incisions. The use of other therapeutic measures is only of value where the process is not tuberculous, *e.g.*, the salicylates in rheumatic pleurisy. In general the tuberculosis should be treated as above outlined.

4. TUBERCULOSIS OF THE LARYNX

I have never seen a primary tuberculosis of the larynx; secondary infection, however, is common in older children. This complication is evidenced by a roughness or hoarseness of the voice. Laryngoscopic examination shows a profuse redness and swelling about one or more ulcers or tubercles. The pain is frequently marked and interferes with swallowing and nutrition. The cough may be very troublesome. The ulcers can be confused only with syphilitic affections. However the presence of the pulmonary condition in tuberculosis as well as the sharply circumscribed nature of the syphilitic ulcers serve to differentiate the two.

Treatment consists of mild applications of lactic acid. Cocaine is used to relieve the pain.

SCROFULA

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SCROFULA is a disease of childhood, and of puberty, occurring somewhat more often in the female than in the male sex.

The name "Scrofula" is derived from Skropho, I root; and signifies a young swine. The basis for this term was very likely suggested by the striking disfigurement of the face and neck occurring in typical cases, and which indeed reminds us of the appearance of a pig.

Historical.—At the beginning of the last century, the name scrofula was very often used synonymously with tuberculosis. Lænnec considered scrofula nothing more than a tuberculous disease of the glands and in this conception had many followers.

Virchow combated this opinion. For him, the tubercle alone is characteristic of tuberculosis, not the caseous degeneration upon which Lænnec laid special weight, since this may occur also in other conditions, as cancer, etc.

The scrofulous affections, according to Virchow are "irritative changes in the tissues, which have, partly, a hyperplastic, and partly an inflammatory character." Scrofula in the narrower sense, he considers a disease of the lymphatic nodes, which is provoked by a certain weakness, or imperfect structure of the respective glandular regions.

The discovery of the tubercle bacillus by Koch, led to the positive proof, that joint and bone disease, lupus, scrofuloderma and lichen scrofulosum are of a tuberculous nature, and hence belong properly under the general term, tuberculosis, and must be distinguished from scrofula. That this distinction is not always made is to be explained by the fact that these diseases were known for generations by the very name of scrofula, and are still believed to be scrofulous changes by the laity.

The lymph-nodes, considered diagnostically so very important in scrofula, showed tuberculosis not only in the nodes presenting histological changes, but in addition the nodes that were simply enlarged could be proven to be infected with tuberculosis in cut sections, and especially by the serum test. Here ought to be added, that since the admirable researches of Bartel and of the Weichselbaum School, there can no longer be any doubt that a lymph-node infected by tuberculosis need not always show specific tuberculous changes.

Even though it is quite generally admitted that the above-mentioned affections, as well as the scrofulous lymph-nodes are of a tuberculous nature, still, the affections of the skin and mucous membranes are not always so considered. These latter affections do not as a rule, show tubercle bacilli, and for that reason, as many authors assert, cannot be classed as tuberculous. Cornet believes that the changes in the skin and mucous membranes are caused not only by the tubercle bacilli, but also by the presence of pyogenic bacteria, such as the staphylococci and streptococci. Still it is not quite clear why these infections in children lead to such severe and stubborn changes; as do not take place in similar bacterial infections.

We will now discuss the indistinct theory called *Predisposition to Scrofula;* an expression which is less often applied to other diseases, or is the subject of so much contention and insufficient explanation. Even the views of Virchow as referred to above, contained such ideas on this subject, without telling us of what the assumed weakness or insufficient functions of the respective lymph-nodes consisted.

Cornet in his well-known work on scrofula, devoted an entire chapter to predisposition to scrofula, and explains its cause in the greater permeability of the skin and mucous membranes, to bacteria, and the greater number of lymph-passages. He tries to prove that this permeability in the organism of the child, as compared with that of the adult, is naturally greater, and is enhanced in certain individuals, furnishing thus the predisposition to scrofula. He calls this condition Increased Infantilism or Embryonalism. Unfortunately however, anatomical findings are lacking to verify this embryonal condition in scrofulous individuals. While Cornet completely rejects the theory of a predisposition affecting the entire human system, Czerny endeavored to find this predisposition in the chemical composition of the organism, asserting that for a predisposition to infectious diseases, we must assume an alteration of the chemical compositions of the body. But no chemical examinations to substantiate this theory have as yet been made. It may be here briefly mentioned that Czerny's idea differs greatly from the generally accepted conceptions of scrofula. Only that which can be proven histologically or bacteriologically as tuberculous is actually tuberculosis and is to be distinguished from scrofula. Czerny's definition of the term scrofula did not lead to a clearer understanding, nor to a better classification of the affection; on the contrary, an old name, which, heretofore, was applied to other conditions, was made to serve as a name for a sympton-complex. Recently however, Czerny has renounced the name scrofula, for his special series of symptoms and classified the respective signs in accordance with his new theory, under the name "exudative diathesis," which will be spoken of in another part of this book. It must be mentioned here, that a part of the patho-

logical phenomena, arranged by Czerny under the name "exudative diathesis," are still embodied under the old name scrofula. Others however, may be believed to be conditions, which, according to Heubner, could be called Lymphatismus. Czerny's ingenious interpretations show very clearly our perfect ignorance of what the real nature of this diathesis actually is. Classify these conditions as one will, future chemical examinations may show better criteria; until then we must be content with such terms as: "peculiar tendency," "diathesis," etc. That hereditary influences may play an important part in the development of "scrofulous tendencies," is perhaps universally acknowledged. And indeed, it will be noticed, that those children are mostly attacked by scrofula, whose parents had the same disease or tuberculosis in their youth, and the appellation, "scrofulous families," as used by the people at large must be acknowledged as justified. As has been noted laymen even now consider tuberculosis of the joints, bones and skin as manifestations of scrofula.

Owing to the extraordinary influence of heredity, Soltmann made an attempt to explain the predisposition to scrofula and the tendency to tuberculosis in such individuals, and it is worth while to mention it. Before I consider this theory, I wish to state that "heredity in tuberculosis" will be treated in the chapter on tuberculosis. Soltmann assumes that not the actual bacilli enter into the fœtus, but rather the toxins produced by the tubercle bacilli, and these toxins, passing through the placenta, poison the developing organism. The result of such poisoning it is believed, is the cause of a scrofulous constitution with a tendency toward acquiring tuberculosis. The diathesis would have to be at once diagnosticated as a sign of tuberculosis, in the sense of a toxic infectious disease, and the tendency for such individuals to take tuberculosis, would be nothing more than an over-sensitiveness of the already poisoned organism to the tuberculous virus—a theory well shown in this disease from our knowledge of tuberculin.

Of course all this is only hypothetical, and as yet entirely unproven, inasmuch as it presupposes the circulation of tuberculous toxines in the body of the pregnant mother. This is hardly a plausible assumption. But suppose we were inclined to reject such a direct influence as heredity, we must still admit that children of tuberculous parents are very frequently subjected to the possibility of infection from tubercle bacilli and for that reason very frequently become ill; even this opinion is not to be accepted without reserve for not all parents supposedly afflicted with tuberculosis, and whose children fall ill with scrofula, have tuberculosis in such a form as to infect their surroundings with tubercle bacilli.

It must be remembered, that in recent times, the view expressed by von Behring on the subject of infection by tubercle bacilli in nurslings is receiving greater confirmation, but it does not by any means

follow that a true case of tuberculosis results, instead it often happens that the infection remains latent. Under such circumstances the development of a case of scrofula is a sign that an infection with tuberculous virus has taken place.

All these speculative arguments make it clear that at present there is no explanation for the hereditary influence that undoubtedly exists; in other words we must accept the theory of an hereditary predisposition although nobody can tell in what it consists.

The question now arises, What are the relations of the individual symptoms of scrofula to tuberculosis? It has been said that so far as the glands are concerned, their tuberculous nature is generally conceded, but opinions differ greatly as to the conditions found in allied inflammations of the skin and mucous membranes. It is true that in such cases tubercle bacilli are not found, but a great variety of other bacteria, as staphylococci, etc. Such bacteria when found on the surface of the skin and mucous membranes, prove nothing at all. At best, they may be of secondary importance, inasmuch as the inflamed and diseased surface facilitates or favors their penetration. That the staphylococci, etc., may cause suppuration and abscesses, is readily understood; but it is not by any means evident that the symptoms diagnosticated as scrofula are caused by these bacteria. On the contrary, this is even highly improbable, for true infection with pus cocci in a young child shows different characteristics. Compare for instance the course of a scrofulous disease of the eyes, as described below, with the suppurative condition. In the latter we do not find a circumscribed focus, the vesicular eruption, but a diffuse catarrh, accompanied by an abundance of secretion. The prototype of this condition is the gonorrhœal inflammation, which never, even in most stubborn cases, assumes anything like the characteristics of a scrofulous eye. The same may be said of other pyogenic agents, the staphylococci, for example. Inflammations present a good opportunity to study such infections of the eye, manifesting themselves by a deficient winking and closure of the eyelids in severe intestinal affections. In case we succeed in keeping such a child alive, the ocular suppuration may extend over the entire period of convalescence, which may last for weeks, but it never assumes such characteristics as might cause it to be confounded with scrofulous disease of the eyes.

It is the same with affections of the skin and mucous membranes. Infections of the skin with staphylococci lead to the formation of furuncles, to abscesses and to inflammation and suppuration of the glands involved, but they do not produce that peculiarly stubborn scrofulous catarrh, tending toward a state of hyperplasia and ulceration. We may observe in a poorly nourished child afflicted with chronic intertrigo a great many skin affections in conjunction with suppuration, but no

changes characteristic of scrofula. Hence it is quite an arbitrary assumption to confound the scrofulous diseases of the skin and mucous membranes with infections by bacteria and especially the pus cocci.

To explain this we must again resort to predisposition, a peculiar but unproven anatomical condition. But even granting such a peculiar anatomical condition, and such a singular disposition on the part of the tissues, there still remains to be explained the theory why it is that in these individuals with such peculiar disposition, bacteria of absolutely different biological effectiveness, as tubercle bacilli and pus cocci, produce at once the same anatomical changes, which they otherwise never do as a rule.

It must not be inferred that tubercle bacilli are not present, because pus is produced, or because they cannot be found. Heubner in his text book, teaches as follows: The peripheral appearance of scrofula is immediately succeeded by an infection of the glands with tubercle bacilli, and it is inconceivable, why these catarrhs should only furnish the opportunity for the entrance of tubercle bacilli, nor is it quite clear, why this occurs just here, and not in other inflammatory conditions of the same organs. Moreover, it must be emphasized that nearly all scrofulous children and even those who do not yet show any glandular swelling, react with tuberculin and also possess in their serum the power to agglutinate tubercle bacilli.

Finally, we regularly find as Heubner says, in necropsies of such cases of purely scrofulous catarrhs, tuberculosis of the bronchial glands. It is more sensible therefore, because of the close connection existing between scrofula and tuberculosis, to ascribe even these peripheral affections to the latter, insead of to something else which nobody has seen nor proven.

It has also been observed in children, with pronounced tuberculosis, that typical scrofula suddenly appears. It has been mentioned above that latent cases of tuberculosis, can, by biological investigations, be detected even in very young suckling babies, and we must repeat the assertion, that when scrofula later develops it is nothing else but evidence of the already existing infection.

Therefore, it appears to me correct, to believe strongly that these scrofulous catarrhs also are tuberculous in nature.

DISEASES OF THE EYE

Lymphatic conjunctivitis or keratitis, *i.e.*, scrofulous or phlyctænular keratitis, is a localized disease, distinguished from all other inflammatory affections of the conjunctiva, and representing rather a diffused catarrh of the connective tissue.

The disease begins with the appearance of a conical vesicle in the limbus, together with fascicular, and radiating vascular injections. At

the top of the cone an abscess forms, which spreads until it reaches the conjunctiva, and then goes on to a cure. Usually there are a number of vesicles which may develop beyond the limbus, and even on the cornea. These little nodules or abscesses often heal in about a fortnight, but relapses are very frequent; in fact almost the rule, so that the disease, first attacking one eye, then the other, may trouble a patient for years. The vesicles of the cornea may heal without opacity, but, on the other hand, deep abscesses do occur, permeating Bowman's membrane, which can only heal with permanent opacity. Furthermore the ulceration on the cornea may assume a serpigenous character and accompanied by vascular adhesions may cover larger or smaller areas of the cornea. Within the confines of this vascular adhesion permanent opacity regularly occurs. Finally instead of a localized affection, a diffuse neoplasm, which is known as "Pannus scrofulosus corneæ" may develop. This neoplasm is generally thin and capable of disappearing.

Photophobia is the subjective symptom of paramount importance. It is nearly always present and severe in form; less frequently it is of a mild character. The children retire into dark corners, lie down on their faces, press their heads tightly into the pillows and resist most energetically any attempt to open their eyes. The blepharospasm may reach so severe a form that it is impossible without resorting to the use of the speculum to see the condition of the eye. As a result of the inflammation there is a profuse flow of tears. On account of the almost constant moisture on the lids, blepharitis in an intense form develops, in consequence of which an irregular position of the cilia as well as eczema of the eyelids may be observed. This latter condition may in permanent cases become so intense, that it may lead to deformity or eversion of the lids, *e.g.* ectropion. In addition to this in long standing cases as a result of the constant irritation of the tears, a diffuse inflammation of the palpebral conjunctiva may occur. This inflammation as such has nothing to do with the real scrofulous disease of the eye. In summing up all of the evidence we come to the conclusion that the disease is founded upon a localized affection of the exterior coverings of the eyeball. Its stubbornness, and the repeated relapses, indisputably characterize its scrofulous nature. Whether the chronic diffuse inflammation of the lids, skin, etc., which arises in consequence, is caused by recurrences of the scrofulous disease of the eyes in particular, or by a special vulnerability of the tissues in chronic scrofula (habitus scrofulosus) must still remain a mooted question. The prognosis of the ocular affections is in general a favorable one, particularly, if the severity and long duration of the pathological phenomena are taken into consideration. In the majority of cases there occur only slight permanent injuries to the power of vision. Serious disturbances or total blindness are very rare.

DISEASES OF THE NOSE

With very few premonitory symptoms a patient is attacked by a severe and remarkably obstinate chronic cold in the head. There is a marked swelling of the submucosa. A limited quantity of a sticky mucoid secretion appears, which however soon dries up forming a crust and soon leads to intense irritation of the skin and to excoriations in the nasal orifices. The irritation of the neighboring skin, particularly of the upper lip, causes the appearance of a *chronic eczema,* which at first does not differ from any other eczema, but later assumes a peculiar character of its own on account of its great obstinacy and the chronic swelling of the affected parts which appears in consequence of the infiltration of the subcutaneous connective tissues. The pernicious effects of the diseased eyes, described above, together with the consequences arising therefrom, give the face that repulsive appearance, peculiar to scrofula, and which in reality reminds one of the appearance of a pig (see Plate 39). Of course the secondary changes of the skin arising from the ocular disease and the rhinitis may assume different aspects. The eczema is apt to spread over the entire face and the hairy scalp as well, forming thick crusts. Furthermore, through infection of the eczematous skin, multiple abscesses and ulcers may form which stubbornly resist all measures used for their cure. Frequently the eczema extends to the external auditory canal. The result is an intense otitis externa, with much swelling of the auditory canal and copious formation of crusts often completely obstructing the external auditory canal. This condition be it observed, may occur without an accompanying otitis media; though in many cases this does exist and through its secretions there may result eczema of the auricle and the auditory canal.

OTITIS MEDIA

Whether otitis media may be directly accepted as a symptom of scrofula, as is often done, or not, is a matter of opinion. Otitis media is a very frequent disease of childhood. It is often noticed in children that show no signs whatever of scrofula. The condition can easily be accounted for by the constant possibility of infection from rhinitis. But at the same time it cannot be denied that this disease of the ear proves to be just as obstinate as other affections pronounced as scrofulous; nay more, it clings to the patient even after the disappearance of scrofula proper. It continues into the later period of childhood and not infrequently results in very serious afflictions. Chronic otitis media may result in serious affections of the antrum, and of the mastoid process. However these affections do not differ from those occuring in non-scrofulous individuals. There is also a scrofulous otitis, having its origin in an infection with tubercle bacilli. Swelling and caseation of

I II

Scrofula.

I. Case from the Berlin Children's Hospital (Professor Heubner).
II. Case observed by Professor Schlossmann.

the regional lymphatic nodes, tuberculous disease of the bones, caries of the petrous portion of the temporal bone, etc., can be found in such cases.

AFFECTIONS OF OTHER MUCOUS MEMBRANES

It must be mentioned in relation to affections of other mucous membranes, that some writers believe that the chronic hypertrophic inflammations of the nasopharnyx and adenoid vegetations belong to scrofula. This however cannot be admitted. Chronic swelling of the lymphatic tissues in childhood, which is especially prone to arise in cases of adenoid proliferations, is a matter of such frequent occurrence in early life in cases with no suspicion of scrofula about them, that it cannot be conceived how these two conditions can be confounded with one another. We are here dealing with a clinically well known aspect of a disease which is so successfully called by Heubner "lymphatism." It may briefly be mentioned here that the chronic swelling of the lymphatic nodes, which may be placed in the category with the adenoid vegetations, never show tuberculous characteristics, while on the other hand, the tuberculous nature of the scrofulous glands can hardly be doubted.

THE SCROFULOUS GLANDS

Diseased cervical lymphatic glands are very frequently observed and most easily diagnosticated (see Plate 39). At first enlargement of a single or several glands takes place at the angle of the jaw, before or behind the sternocleidomastoid muscle. This swelling spreads more and more until an entire chain of glands is involved.

The hypertrophy extends gradually and without much pain. It may become so extensive that large tumors are formed on both sides of the neck. This disfigurement along with the chronic inflammatory swellings of the face changes the countenance, giving it the peculiar appearance of a pig (see Plate 39). The tumors formed often remain firm for a long time, but on the other hand they frequently soften and suppurate. They may, through an inflammatory process become hard and adhere to one another, and to the skin. The skin over the softened glands becomes œdematous, tense, then shows a bluish discoloration, gets thinner and at last the gland discharges.

Fistulas may form from which there is a discharge of a whitish flaky and purulent fluid, mixed with curdy material. The fistulas are apt to develop into ulcers, which resemble tuberculous ulcers and stubbornly resist treatment. Similar phenomena may appear in all other glandular regions although they are less frequently found in other localities.

The nature of the glandular infection is still to be considered. There is hardly any doubt to-day that all scrofulous glands are infected with tubercle bacilli. It is by no means necessary that every infected

gland should show changes which are anatomically of a tuberculous nature. Recent researches, particularly Weichselbaum's, have taught us that virulent tubercle bacilli may be present in the medullary substance of the swollen glands. As a matter of fact because of the chronic eczema still other bacteria may penetrate to the glands and cause abscesses. However this is only accidental and has nothing to do with the scrofulous process proper. Of course we see in cases of chronic eczema, especially in eczema of the face and scalp of nurslings, considerable swelling of the regional glands; but they never manifest the changes described above. They hypertrophy and undergo a process of involution, or if they soften, they simply merge and form a simple glandular abscess. Nobody would call such glands scrofulous, for they are in every case liable to infection; and this is true not only in children, but in adults.

If one would regard every case of chronic eczema in young children as scrofula, then he might likewise call these glands scrofulous, but the whole conception of scrofula would be shifted thereby.

DISEASES OF THE BONES AND JOINTS

The so-called scrofulous diseases of the bones and joints most assuredly pertain to the class of tuberculosis and a discussion of them in these pages is only a concession made to the old term "scrofula," to which those diseases are supposed to belong.

The limited space which could be devoted in this manual to the subject of scrofula only permits a brief statement of the general pathology and symptomatology of the subject. For details we must refer the reader to the text books on surgery.

The tuberculous diseases of the bones nearly always appear as a secondary disease, originating through infection from some existing localized area. The structure of bone marrow is such that tubercle bacilli circulating in the blood are easily arrested, and these subsequently lead to the formation of tubercles in the bone marrow. The tuberculous granulation-tissue liquefies the bony structure, and may lead to necrosis, or to the formation of a sequestrum. It spreads centrifugally, producing a state of caseation. This process may extend peripherally to the periosteum and cause a tuberculous periostitis. A cold abscess may now result, the process including the overlying soft parts. Fistulas may arise and discharge externally.

If the softening of the bone is accompanied by enough resistance on the part of the periosteum, then a peculiar spindle-shaped swelling results, particularly in the phalanges of the fingers which is known by the name of spina ventosa. Since the tuberculous affections are inclined to remain in the neighborhood of the articulations, the extension of the process to the joints is easily explained. Primary involvement

of the joints is rare. In the joint there develops an exudate of a serous or even seropurulent nature. Gradually the synovial membrane changes to spongy granulation tissue, which, penetrating the cartilage, destroys it, and detaches it from the bone. By degrees the process spreads over the soft parts, they swell, become œdematous, the surface turning white and glossy, and the whole joint presents a spindle-shaped swelling known as tumor albus or white swelling.

Other diseases of the bones, spondylitis for example, are at present generally separated from scrofula and for that reason must be studied elsewhere.

The process in the localized bone diseases is extraordinarily slow and tedious. At first there are no symptoms, then from time to time mild pains, especially at night, are felt. Gradually these pains become more severe, function is disturbed in the beginning and finally is rendered impossible. By this time objective changes are noticeable, such as have been described above.

Prognosis.—The prognosis of scrofula is, in general, favorable. The scrofulous phenomena themselves never result in death. They finally heal though they may frequently last for years without leaving any marked functional disturbances. Serious disturbances may however threaten the eyesight, as has been already explained.

But the prognosis assumes a different character when we consider the relation of scrofula to other tuberculous phenomena and to certain diseases. We must accustom ourselves to regard the scrofulous individual as infected with tuberculosis, in other words to have an infectious disease; which for the time is quiescent and not dangerous, but is apt at any time to assume such a rôle under favorable conditions. Such favorable conditions are unhygenic surroundings and malnutrition. A scrofulous child thus exposed is in great danger.

Instead of suffering from a comparatively harmless form of scrofula it may acquire a severe tuberculous affection jeopardizing permanently its health and life. In many cases re-infection may occur if the child is associated with a phthisical subject.

There is hardly any doubt that the form of tuberculosis, whose symptoms are grouped under the name of scrofula, creates in the organism a certain sensitiveness and susceptibility to re-infection. Our present biological knowledge teaches us that there is a hypersensitiveness to the virus in question, which can be distinctly proven by the reaction produced by the smallest doses of tuberculin.

This inclination to tuberculous infections which positively exists in scrofulous children, teaches us of course, that the prognosis in this respect depends entirely upon whether a child is obliged to live with a person afflicted with phthisis, or whether measures are taken in time to remove it from its dangerous surroundings.

The scrofulous organism is already infected with the virus of tuberculosis and if its power of resistance is further weakened by unsanitary surroundings or by unhealthy and insufficient food, the original infection may then assume more dangerous forms.

The relation of this statement to the prophylaxis and therapeutics of scrofula will be explained below. Besides the two etiological factors mentioned, it is still necessary to consider a few other agents active in the development of severe cases of tuberculosis. Any of the infectious diseases will attack the scrofulous organism more violently than the healthy one; in particular measles and whooping-cough are to be most feared. Both of these infectious diseases greatly favor the transformation of a latent mild case of tuberculosis into a florid and severe one. Consequently scrofulous children who have the misfortune to acquire either of these two maladies, are to be regarded as in great peril.

All the consequences resulting from unhygenic surroundings, association with the tuberculous, etc., as mentioned above, are doubly effective under these circumstances, and in case it is not possible to remove these pernicious factors thoroughly and quickly the prognosis is strongly influenced for the worse.

The danger in the complication with measles is present not only during its brief acute period, but even after this infection is past, so that children who have had the measles under good hygenic conditions, for instance in a hospital, must be still protected from all injurious influences. Whooping-cough which may last for months, endangers the patient during the entire period of its course.

Prophylaxis.—We can hardly discuss the prophylaxis of scrofula because the mode of its origin is unknown to us. Even from the viewpoint that every case of scrofula is founded upon an infection with tubercle bacilli, it still remains unexplained where this infection has taken place. If we accept the theory of the inheritance of scrofula—a theory which according to most recent researches cannot be rejected—then prophylaxis is impossible. In the majority of cases however, the infection may possibly take place outside of the uterus, then naturally precautionary measures against such infection may be taken.

The more we are inclined to share von Behring's point of view that tuberculosis acquired in the earliest period of life may for a long time remain latent, the more we are forced to believe that young babies should at once be removed from any association with the tuberculous, and that children whose parents have active tuberculosis should be separated from them as soon as possible. Among the very poor the removal of the infant means at the same time a departure from unhygienic surroundings which favor an infection with tubercle bacilli and an outbreak of scrofula. Such prophylactic measures can very easily be carried out with illegitimate children. With legitimate children the

problem is more vexatious. Only rarely will parents make the sacrifice of an early separation from their child.

Attention must be called to the fact that sanitary improvements in the housing of the poor are everywhere necessary and that scrofula and tuberculosis could be more successfully combated by such supervision. In this respect the prophylaxis of scrofula and tuberculosis so completely harmonize that a special discussion is superfluous. We must refer the reader to the article on tuberculosis.

Therapeutics.—Primarily remove all those pernicious influences which have been mentioned under prophylaxis. Narrow, damp and badly lighted dwellings must positively be avoided. Among the poor these precautions can but seldom be observed; and it may in these circumstances be advisable to place the child in a well organized institution. In addition to other therapeutic measures, of which we will presently speak, it is evident that improved hygienic conditions alone will have a far reaching influence upon the condition of the suffering child.

It is self-evident that only such hospitals for children are considered here as have been built and organized in accordance with the principles of modern hygiene. It is a most gratifying fact that much has been done to meet these demands. Well organized homes and hospitals for children have been erected, and in the large cities there are ever-increasing movements afoot to further these humane endeavors. Plans have been made to send children to the country into the open air: forest recreation retreats, and forest schools have been established for them.

Another requirement in the general therapeutics of scrofula is sufficient and suitable nutrition for the children. Among the laboring classes the food is often insufficient and inadequate, and it is of the greatest importance in the treatment of scrofulous children to take good care of their nutrition. It is by no means necessary, nay, not even desirable, that the diet of such children should be principally nitrogenous. It is desirable that carbohydrates predominate: potatoes, white bread, green vegetables, rice, etc., should be given. Fats should be used for the scrofulous as a source of energy. I would not advocate avoiding or limiting it as Czerny teaches. Fat is for such children no more injurious than for children in general. The fat is to be supplied in the form of butter, cream, and milk. Undoubtedly codliver oil, that well-known and popular remedy, is indebted for a great share of its effectiveness to its fatty properties. Fresh fruit should also be included in the child's dietary. An exclusive milk diet is not recommended, in its stead a diet of good fresh vegetables alternately with milk is more suitable for the scrofulous patient.

Further general therapeutic results are obtained by stimulating the activity of the skin, the circulation, the respiration and the heart.

For this purpose salt and brine baths are very popular and pleasant. For stout, flabby children who are frequently found among the scrofulous, such measures may prove of great advantage. By this means stimulation or acceleration of metabolism is produced, and without doubt an improved appetite, an increased vivacity and a better natured child results. It is necessary however to select carefully the children suitable for this treatment. Children who have been brought up in wretched circumstances and as far as nutrition is concerned have known nothing but want and misery, are completely unsuited for such a plan of treatment. Such children also require stimulation of their circulation, increased skin activity as well as exercise to increase their powers of resistance, but the measures used to attain such results must be milder and comparatively gentle in their application. Of this we shall speak hereafter.

In general it may be said that brine and salt water baths are used too promiscuously. The method of giving the bath is simple: from two to four pounds of salt are added to the bath, which is to have a temperature from 95° to 98° F. The child is kept in the bath from five to ten minutes, the surface of its skin being lightly massaged when taken from the bath, the patient must be quickly dried with absorbent towels, quite vigorously rubbed and wrapped in warm blankets. The patient is then kept in bed for about an hour. If such baths are not available, similar treatment may successfully be resorted to by inunctions of soft soap. Every day for five minute periods, the back of the body is rubbed with green soap applied with soft cloths, from the neck to the buttocks, and from the thighs to the popliteal space, and then washed off with lukewarm water. If the skin becomes irritated, it is well to omit the treatment for a few days. This treatment may be continued from six to eight weeks, and again resumed after an intermission of from four to six weeks. The success attained by such an inexpensive and simple method is very often remarkably good.

In case we are obliged for reasons that have been mentioned above, to refrain from too active skin stimulation, then a gradual process of hardening the body may be employed. We begin with dry frictions of the whole body, once or twice a day of ten to twenty minutes' duration, and continue this process for two or three months. Then lukewarm ablutions may be started, passing gradually to baths and massage at a cooler temperature.

But we must be extremely careful not to apply any severe processes of hardening to feeble scrofulous children, or to those suffering from the so-called erethistic type of scrofula. The patient's condition often becomes much worse with such inconsiderate treatment, and an aggravation of the anæmia is the disagreeable consequence of such faulty management.

To assist these therapeutic measures, climatic treatment can be added with great success. Sea baths are mostly in vogue. Unfortunately the right methods are not always applied. As regards the feeble, poorly nourished and anæmic children, a sojourn at the sea-shore must certainly be beneficial. We must recollect that a sojourn at the sea-side is unquestionably of greater benefit than a stay in an inland region with good, pure country air. For children strong enough to endure the invigorating effects of sea climate, a residence on the coast may prove a powerful curative factor. Of course such a visit must not be too brief. Cures lasting four, six, or eight weeks, almost always improve temporarily the general condition of the patient but rarely have a permanent effect. A sojourn of four to six months, or even a year or more is required to secure proper permanent results. The winter seasons especially are too little used. The fresh pure air of the sea-shore, a fairly even temperature with rarely an excessively cold day, fit it particularly for a winter residence. In America, the well-to-do patient can make a protracted stay at several places on the sea-shore, during the winter season, for there are places which offer good accommodations and even medical attendance. For the children of the poorer classes, charitable organizations are beginning to make the sea-shore accessible and profitable. A rest at the sea-shore of four or eight weeks at most may result in temporary, but not permanent benefit. After his speedy return to unhygienic conditions, the advantages acquired are soon lost and the relatively expensive sojourn has done little for the child except to indicate the road to recovery without supplying him with the means to reach the goal.

A stay in the mountains is also very beneficial. For the older and stronger children, reasonable winter sports may be enjoyed there. Very feeble, erethistic children are not well adapted for either of these climatic changes. Sparing the body, rather than stimulating it, should be the endeavor in these cases. Such children ought, if possible, to spend the winter in a mild climate.

The foregoing remarks may suffice to throw some light upon the subject of the dietetic and physical curative methods of scrofula in general.

As to *medicinal treatment,* there may be given, codliver oil, syrup of iodide of iron and similar preparations, as guaiacol carbonate 0.1–0.3 Gm. (1½–5 gr.) in powders several times daily, or in codliver oil 3 : 200, a tablespoonful twice daily. Cresotal 6 to 8 drops may be given several times daily.

These drugs can aid in securing the therapeutic effect desired, but can hardly accomplish it alone.

Specific Therapy.—It has been stated above, that nearly all scrofulous children react to tuberculin; and sometimes we see remarkable

improvement, as a result of judicious tuberculin treatment, not only in the localized processes, but in the patient's general condition as well. The treatment should be used only on patients that are free from fever. We begin with $\frac{1}{20}$ to $\frac{1}{10}$ mg. of old tuberculin; or possibly a little more, until reaction sets in; after its absorption, the injection is repeated 8 to 14 days later, with doses as above given, and continued until reaction ceases. Gradually the doses may be increased up to 1 mg. of the old tuberculin. After this a longer intermission may be allowed, in order to resume the treatment at the end of a year or later. In Heubner's clinic a few cases came under my observation, showing remarkable improvement, and at a later period complete cure.

Eyes.—Calomel powder, and yellow precipitate ointment, once a day. A contraindication is the presence of new infiltrates or progressive ulceration. In these cases apply atropine until the inflammation has disappeared. With larger ulcers, and extensive corneal infiltrations (suppurative keratitis) apply moist warm poultices several times daily for one to two hours. Bandages are only to be used if the corneal ulcers are large, otherwise it is better to do without them.

Eczema occurring with scrofula is to be treated in accordance with prevailing methods. For details on this subject, consult the chapter on skin diseases. Scrofuloderma is most favorably influenced by tuberculin treatment. Internally, arsenic has been recommended. If ulcerations are present, local applications of balsam of Peru, nitrate of silver, etc., may be resorted to, *e. g.* in the following form:

Argenti nitras	0.3,	grs. v
Balsam Peru	3.0,	♏ l.
Vaseline	30.0,	℥ i.

Furthermore scraping with a sharp spoon, cauterizing, or surgical treatment may become necessary. Lichen scrofulosorum hardly needs special treatment. For this disease, inunctions with codliver oil are indicated.

Glands of the neck are accessible to the knife, and it would seem reasonable to remove localized tuberculous tumors. It is true that prominent surgeons (Hueter) have earnestly advocated such treatment. However, the removal is somewhat dangerous, for in the first place, the operation means more or less loss of blood, to which young children in general are very sensitive and particularly the scrofulous who are poorly nourished and anæmic. Secondly, it is extremely difficult to make a complete removal and thereby avoid a recurrence of glandular hypertrophy (von Bergmann). Thirdly, experience teaches us, that tuberculous meningitis, or general miliary tuberculosis may follow the extirpation of the glands. For this reason it may be more judicious not to treat scrofulous glands surgically, except those very

large disfiguring tumors, which are making firm pressure upon important organs. Necrosed glands and other invasions originating from them, must, as a matter of course, receive surgical treatment.

Bones and Joints.—Extreme conservatism is recommended here. Immobilizing dressings, and Bier's passive hyperæmia, must be mentioned. For particulars on the subject consult the text books on surgery.

SERUM DISEASE

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Although it had frequently been observed that the introduction into the human organism of heterogeneous blood produced symptoms of illness, it is only since the universal adoption of serum therapy in diphtheria, since the injection of horse serum in thousands of cases, that this observation has become of real significance. At first it was thought that the strength of antitoxin in the serum was responsible for the symptoms following its use, until Heubner, von Bokay and Johannessen proved the heterogeneousness of the serum to be the cause.

Much depends on whether the serum is injected for the first time or repeatedly.

SYMPTOMS FOLLOWING THE FIRST INJECTION

The injection of the serum causes according to its quantity a smaller or larger swelling, which is more slowly absorbed than an equal quantity of physiological salt solution. But as much as 200 c.c. are perfectly absorbed within twenty-four to forty-eight hours. Aside from a slight discomfort at the site of injection no changes are apparent during the first few days.

The small quantities of diphtheria serum employed to-day produce clinical symptoms in only 5 per cent. of cases, although in every case there are biologic changes going on in the organism, of which we shall speak in connection with reinjection.

In typical cases the symptoms of serum disease begin to appear eight to twelve days after injection.

There may be slight prodromal symptoms, as transitory redness, sensitiveness of the skin of vasomotor origin. A more constant and early symptom is the swelling and tenderness of the regional lymph-glands continuing throughout the disease without ever going on to suppuration. Usually the first symptom we notice is a breaking out of urticaria, originating at the site of injection where it sometimes remains localized.

The eruption, accompanied by intense itching, varies greatly in size and shape, changing from disseminated small wheals surrounded by a red border to large urticaria infiltrations as large as the palm of the hand, and tend to spread quite rapidly over the entire body. Each individual wheal is of short duration, but for a number of days there appear successive crops.

As a result the face is often greatly swollen, general œdema may be present, not sufficiently marked to be apparent, although its presence may be proved by weighing the patient, when an increase of several pounds may be found. The œdema is not of nephritic nature, for only exceptionally do we find albuminuria, never nephritic elements in the urine.

Inflamed areas seem predisposed to œdema, at least œdema of the larynx after it has disappeared is sometimes seen to recur at the time of the urticaria eruption and may produce symptoms of laryngeal stenosis (subglottic œdema of Mya).

The knowledge of this fact is of great practical importance, because otherwise one is inclined to regard the reappearance of the stenosis as a recurrence of the croupous process and to again inject serum which would only aggravate the condition. Intubation, however, is not contraindicated. The prognosis is good; with the disappearance of the serum disease the laryngeal stenosis subsides.

The eruption of urticaria is accompanied by a moderate rise in temperature, only exceptionally is a high temperature observed. The type of the temperature is remittent; the exanthem may, however, occur without temperature, although more frequently the opposite is the case, where we notice a rise of temperature without other symptoms of serum disease (*formes frustes* of Lehndorff).

The mild cases lasting generally but a few days are almost entirely free from constitutional disturbances. The patients feel ill only when the joint pains appear, which are supposed to be due to changes in the synovia analogous to the exanthem.

More severe constitutional disturbances occur in cases where the serum disease is of long duration following the use of large doses (50 to 400 c.c.) of horse serum. In these cases we may also notice rarer forms of exanthems following one another, the most important being the one resembling measles and the *erythéme marginé aberrant* (Marfan) resembling the erythema multiforme of the other types of the exanthem, only the erythema resembling scarlatina is of some importance. It is really quite rare; most cases of supposed scarlatinoid serum exanthem are cases of genuine scarlatina. The diagnosis should therefore be made cautiously.

The diagnosis of scarlatina is positive in the presence of marked redness of the mucous membranes of the mouth and throat, for the mucous membranes in these places are never involved in serum disease. The conjunctiva, the bronchial and intestinal mucous membranes may in rare cases be involved, a slight catarrhal condition being the result.

SYMPTOMS FOLLOWING REINJECTION

Repeating the serum injection within ten days after the first injection does not produce symptoms which differ from those following the first injection. But if reinjection takes place in intervals of twelve days

to four months, we very frequently see the symptoms of "immediate reaction." Contrary to the first injection the symptoms of the disease appear within the first twenty-four hours, not infrequently a few minutes after reinjection.

The most prominent symptom is the sudden eruption of a general urticaria, with marked œdema of the face and rise of temperature. In several cases there developed with the eruption of urticaria symptoms of collapse (general cyanosis, dyspnœa, small pulse). These grave symptoms remind one of the fatal termination in guinea-pigs which invariably follows the intravenous reinjection of horse serum. Fortunately these symptoms of collapse occur only exceptionally in man. Theoretically it is not at all improbable that an intravenous reinjection could result in death. The fatal cases, however, described in literature at the beginning of serum therapy, do not belong here, because they were cases of first injection.

A more frequent symptom and often the only one following reinjection is a local reaction at the site of reinjection. The subcutaneous tissues become greatly swollen, sometimes within a few hours, the skin is reddened and there is present a faint erythema and tenderness on pressure.

As rapidly as the general and local symptoms appear, so as a rule do they subside.

This, however, is not always the end of the disease, for often, especially after large doses, there is after four to six days a second general eruption of urticaria accompanied by a rise of temperature, which may recur for a number of days.

After a period of over four months from the first injection, the "*immediate reaction*" is not seen, only the second part of the symptoms. As the period of incubation seems to be but half of that of the first injection (which is from 8 to 12 days), this form of serum disease has been called "*accelerated reaction.*" The disposition to accelerated reaction seems to be present for years.

Immediate and accelerated reaction only exceptionally follow the first injection, but occurring almost invariably with reinjection, we may almost with certainty conclude that the individual has at one time been injected with horse serum.

We cannot discuss here the theoretical questions as to the *cause* of the period of incubation and serum disease; we may briefly mention that we believe the cause of serum symptoms to be antibodies.

It is our opinion the action of antibodies on the heterogeneous serum results in a substance which has a disease-producing effect on the organism. After the first injection these antibodies are developed in eight to ten days, the normal period for the development of serum disease; they remain in the body for several months and if a reinjection takes

place during this time, the injected horse serum and the antibodies, which are present, produce the substance which causes the immediate reaction.

After the antibodies have disappeared, the organism is capable of developing antibodies more rapidly after a renewed injection; and although the serum disease does not manifest itself immediately, it appears earlier than after the first injection and thus we speak of an "*accelerated reaction.*"

The antibodies of "*vital reaction*" are not identical with the precipitins which are formed in the human organism following the injection of heterogeneous serum. The laws, however, governing the development of both kinds of antibodies are similar.

The importance of serum disease to the physician should not be overestimated. Fear of serum disease should not prevent one from employing serum in diphtheria. Only when using large doses we should consider whether the disease is so grave as to make even an intense serum reaction of secondary importance. For this reason we employ Moser's scarlet-fever serum, for example, which must be given in doses of 100 to 200 c.c., only in cases with a doubtful prognosis.

A word of warning is in place against the careless injection of serum, especially against superfluous prophylactic injections, as this tends to produce a hypersensitiveness, which is observed when after the development of the disease a therapeutic injection becomes necessary. There is some danger connected with intravenous injection of serum, especially with reinjection, which can prove fatal. The intravenous serum therapy, recently quite strongly advocated (employing serum free from carbolic acid), should therefore be considered only in very severe cases of diphtheria and only in cases to be injected for the first time. It is possible, perhaps, to reduce the hypersensitiveness of those to be reinjected by giving a small dose of serum subcutaneously previous to the intravenous injection. Experiments on animals give encouraging results in this respect.

Serum disease could be avoided if the serum could be given by mouth, or by the rectum, but this prophylaxis would be valueless because, thus employed, the antitoxin would not get into the general circulation.

Various experiments to remove the toxic properties from the horse serum and still retain the antitoxic property, have not proved successful. It is advisable, however, to let the serum settle after withdrawing the blood from the artery of the horse.

The statements of Neter, that the internal administration of calcium salts would prevent serum disease, should be received cautiously as a mere reduction in percentage of cases does not prove much, as serum disease in diphtheria is not of frequent occurrence.

We employ the following symptomatic treatment: In the presence

of tenderness and swelling at the place of injection, applications of liquor Burrowii, warm baths for the extremities. Itching associated with urticaria is relieved by application of a one per cent. alcoholic solution of salicylic acid or menthol. If the temperature is high, cold packs are applied. The use of salicylic acid preparations is followed by a prompt fall of the temperature with perspiration, but the result is only temporary. Salicylic acid preparations have no effect on the joint pains, where we advise warm, moist applications.

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